

Amnesia

ABSTRACTS

- Anon. Effectiveness Of Pycamilon Application For Some Forms Of Cerebrovascular Pathology
- Anon. To The Question Of Pycamilon Application In Complex Therapy Of Acute And Chronic Disorders Of Cerebral Blood-Circulation
- Akhondzadeh S., 1998. Potentiation of muscimol-induced long-term depression by benzodiazepines and prevention or reversal by pregnenolone sulfate.
- Ambrose ML., 2001. Thiamin treatment and working memory function of alcohol-dependent people: preliminary findings.
- Bartus RT., 1981. Profound effects of combining choline and piracetam on memory enhancement and cholinergic function in aged rats.
- Carmel R., 1996. Subtle cobalamin deficiency.
- Cook CC., 2000. Prevention and treatment of Wernicke-Korsakoff syndrome.
- Darnaudey M., 2000. Pregnenolone sulfate increases hippocampal acetylcholine release and spatial recognition.
- DeFeudis FV., 2000. Ginkgo biloba extract (EGb 761) and CNS functions: basic studies and clinical applications
- Diamond DM., 1996. The neurosteroid dehydroepiandrosterone sulfate (DHEAS) enhances hippocampal primed burst, but not long-term, potentiation.
- Diamond BJ., 2000. Ginkgo biloba extract: mechanisms and clinical indications.
- Enrique Gomez, A., 1997. Multicenter study with standardized extract of Ginkgo-Biloba EGB 761 in the treatment of memory alteration, vertigo and tinnitus.
- Kikuchi A., 1999. [A case of Wernicke-Korsakoff syndrome with dramatic improvement in consciousness immediately after intravenous infusion of thiamine].
- Lenegre A., 1988. Specificity of piracetam's anti-amnesic activity in three models of amnesia in the mouse.
- Lindenbaum J., 1988. Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis.
- Masuda Y., 1998. EGG phosphatidylcholine combined with vitamin B12 improved memory impairment following lesioning of nucleus basalis in rats.
- Mathis C., 1999. [Models for the study of memory and neurosteroids]
- Mirzoian RS., 1989. Picamilon Enhances Blood Flow
- Morales AJ., 1994. Effects of replacement dose of dehydroepiandrosterone in men and women of advancing age.
- Ostrowskaia RU., 1985. Antagonism of piracetam with proline in relation to amnesic effects
- Phuaichenko A., The results of clinical study of the drug Picamilon (an analysis of some data of neurologic and psychiatric clinics)
- Pragina LL., 1990. [The effect of piracetam and nicergoline on conditioned-reflex memory under conditions of extreme exposure]
- Racchi M., 2001. Dehydroepiandrosterone and the relationship with aging and memory: a possible link with protein kinase C functional machinery.
- Rakhmankulova IKh., 1985. [Effects of piracetam during prolonged use in an experiment]
- Senin U., 1991. Aniracetam (Ro 13-5057) in the treatment of senile dementia of Alzheimer type (SDAT): results of a placebo controlled multicentre clinical study.
- Shi J., 2000. The effect of 7-oxo-DHEA acetate on memory in young and old C57BL/6 mice.
- Vallee M., 2001. Role of pregnenolone, dehydroepiandrosterone and their sulfate esters on learning and memory in cognitive aging.
- van Wimersma Greidanus TB., 1986. Vasopressin and oxytocin. Their presence in the central nervous system and their functional significance in brain processes related to behaviour and memory.
- Wolkowitz OM., 1997. Dehydroepiandrosterone (DHEA) treatment of depression.
- Yoshikawa T., 1999. Ginkgo biloba leaf extract: review of biological actions and clinical applications.

SUGGESTED READING

Pollina DA., 1997. Amnesia associated with electroconvulsive therapy: Progress in pharmacological prevention and treatment

Genkova-Papazova MG., 1996. Piracetam and fipexide prevent PTZ-kindling-provoked amnesia in rats

Wu C.-R., 1996. p-Hydroxybenzyl alcohol attenuates learning deficits in the inhibitory avoidance task:

Involvement of serotonergic and dopaminergic systems

Hoffmann W., 1983. Effect of mental stimulants on electroconvulsive shock-induced retrograde amnesia

Sara SJ., 1972. Hypoxia-induced amnesia in one-trial learning and pharmacological protection by piracetam.

Schindler U., 1989. Pre-clinical evaluation of cognition enhancing drugs.

Pepeu G., 1989. Nootropic drugs and brain cholinergic mechanisms.

Izquierdo LA., 1997. Systemic administration of ACTH or vasopressin reverses the amnestic effect of posttraining beta-endorphin or electroconvulsive shock but not that of intrahippocampal infusion of protein kinase inhibitors.

Car H., 1995. The effect of vasopressin analogue [d(CH₂)⁵(1),Tyr(Me)₂]AVP on memory process in rats with experimental amnesia.

Effectiveness Of Pycamilon Application For Some Forms Of Cerebrovascular Pathology

Department of Neurology and Neurosurgery, Second Medical Institute, 1, Ostrovityanov St., Moscow 117437, USSR

The pycamilon therapy of 96 patients from 24 to 82 years old with different forms of cerebrovascular pathology has been carried out. The patients have been divided into following groups: ischaemic insultus of hemispheric and trunk localization at the subacute period, bloodcirculation insufficiency in-the vertebro-basilar system with vestibular crisis and transitory global amnesia syndrome, dyscirculatory encephalopathia, vegeto-vascular dystonia, hemicrania, an asthenic syndrome after facile cerebral traumata and neuroinfections. The clinical, neuropsychological, electroencephalographic and reoencephalographic investigations have been carried out. The more pronounced effect of pycamilon has been obtained by therapy of bloodcirculation disorders in the vertebrobasilar system with Meniere's-like and amnestic disorders and also by asthenic syndrome; in the cases of ischaemic insultus and dyscirculatory encephalopathia of II-III degree the effect has been less. - Pycamilon application has been recommended in the supporting doses under ambulatory conditions in the early stages Of encephalon bloodsupplying insufficiency with the irritative debility syndrome and mnemasthenia and also in the asthenic state and hemicrania.

To The Question Of Pycamilon Application In Complex Therapy Of Acute And Chronic Disorders Of Cerebral Blood-Circulation

Military Medical Academy, 6, Lebedyev St., Leningrad 194175, USSR

Pycamilon was found to be effective in 25 patients with insultus and in 28 patients with chronic insufficiency of cerebral circulation. Pycamilon action was studied on the basis of dynamics of the clinical course of the disease, of biochemical, psychophysiological, electroencephalographical and some other results. The positive effect was displayed in the majority of cases, no side-effects were registered. The results of investigation showed, that pycamilon is not only effective but it is the necessary drug in the complex therapy of cerebrovascular disorders. Besides this pycamilon can be used in treatment of different nervous system diseases, accompanied by emotional instability, sleep, memory and attention disorders. Besides vasodilatative and sedative effects pycamilon possesses also antihypoxic properties, that can be used in therapy and prophylaxis of different hypoxic states.

Potentiation of muscimol-induced long-term depression by benzodiazepines and prevention or reversal by pregnenolone sulfate.

Akhondzadeh S, Stone TW. Roozbeh Psychiatric Hospital, Tehran University of Medical Sciences, South Kargar, Iran.

Pharmacol Res 1998 Dec;38(6):441-8

We have recently reported a new protocol for inducing long-term depression through activation of GABA_A receptors in the hippocampal slices. This long-term depression is reversed by bicuculline and potentiated by neurosteroids such as alphaxalone. It was also shown that glutamate receptor activity or extracellular calcium are not involved in the induction of this type of long-term depression. The present study investigated the possible relation between muscimol-induced long-term depression and barbiturates/benzodiazepine-induced amnesia and attempts to determine the possible effect of pregnenolone sulfate on muscimol-induced long-term depression. Extracellular recordings were made in the CA1 pyramidal cell layer of rat hippocampal slices following orthodromic stimulation of Schaffer collateral fibres in stratum radiatum (0.01 Hz). It was observed that pentobarbital, benzodiazepines and pregnenolone at concentrations that did not have any effect themselves on the population spike, potentiate the ability of muscimol to induce long-term depression. In addition to this, the long-term depression was either blocked or reversed by pregnenolone sulfate at concentrations (10 microM) where pregnenolone sulfate did not induce any multiple burst or increase of spike size. The results suggest that the potentiation of this type of long-term depression by benzodiazepines and barbiturates can

explain the main adverse effect of these drugs, amnesia and cognitive impairment. Moreover, the prevention or reversal of this type of long-term depression by pregnenolone sulfate, may suggest a clinical application of this agent in the management of amnesia or dementia.

Thiamin treatment and working memory function of alcohol-dependent people: preliminary findings.

Ambrose ML, Bowden SC, Whelan G. School of Behavioural Sciences, University of Melbourne, Victoria, Australia.
m.ambrose@psych.unimelb.edu.au

Alcohol Clin Exp Res 2001 Jan;25(1):112-6

BACKGROUND: Wernicke-Korsakoff syndrome (WKS) is most often seen in people who are alcohol dependent. Treatment with thiamin may rapidly resolve acute symptoms. However, much evidence suggests that identification of WKS on clinical examination is relatively insensitive when compared with diagnosis at postmortem. No study has investigated the therapeutic effect of thiamin in a sample of alcohol-dependent people without the clinical triad of acute WKS. **METHODS:** We conducted a randomized, double-blind, multidose study of thiamin treatment in 107 subjects who were detoxifying from alcohol. Five groups of subjects were assessed with the Mini-Mental State Examination and were examined for the presence of neurological signs. Subjects were given different doses of intramuscular thiamin for two consecutive days. The posttreatment performance of these groups then was examined on a test of working memory derived from comparative neuropsychology, namely, the delayed alternation task. This test has been established as sensitive to the neuropathology of WKS.

RESULTS: Pretreatment measures of mental status and neurological signs were equivalent across groups. Groups were equated with respect to the background variables of age, education, typical daily alcohol consumption, and years of drinking. On the posttreatment measure, a superior performance was found in the group that received the highest dose of thiamin, compared with the other four treatment groups.

CONCLUSIONS: A therapeutic relationship between dose and working memory performance was indicated. These results have important implications for the management and prevention of WKS, but further investigations are needed to substantiate the nature of the therapeutic relationship.

Profound effects of combining choline and piracetam on memory enhancement and cholinergic function in aged rats.

Bartus RT, Dean RL 3rd, Sherman KA, Friedman E, Beer B.

Neurobiol Aging 1981 Summer;2(2):105-11

In an attempt to gain some insight into possible approaches to reducing age-related memory disturbances, aged Fischer 344 rats were administered either vehicle, choline, piracetam or a combination of choline or piracetam. Animals in each group were tested behaviorally for retention of a one trial passive avoidance task, and biochemically to determine changes in choline and acetylcholine levels in hippocampus, cortex and striatum. Previous research has shown that rats of this strain suffer severe age-related deficits on this passive avoidance task and that memory disturbances are at least partially responsible. Those subjects given only choline (100 mg/kg) did not differ on the behavioral task from control animals administered vehicle. Rats given piracetam (100 mg/kg) performed slightly better than control rats (p less than 0.05), but rats given the piracetam/choline combination (100 mg/kg of each) exhibited retention scores several times better than those given piracetam alone. In a second study, it was shown that twice the dose of piracetam (200 mg/kg) or choline (200 mg/kg) alone, still did not enhance retention nearly as well as when piracetam and choline (100 mg/kg of each) were administered together. Further, repeated administration (1 week) of the piracetam/choline combination was superior to acute injections. Regional determinations of choline and acetylcholine revealed interesting differences between treatments and brain area. Although choline administration raised choline content about 50% in striatum and cortex, changes in acetylcholine levels were much more subtle (only 6-10%). No significant changes following choline administration were observed in the hippocampus. However, piracetam alone markedly increased choline content in hippocampus (88%) and tended to decrease acetylcholine levels (19%). No measurable changes in striatum or cortex were observed following piracetam administration. The combination of choline and piracetam did not potentiate the effects seen with either drug alone, and in certain cases the effects were much less pronounced under the drug combination. These data are discussed as they relate to possible effects of choline and piracetam on cholinergic transmission and other neuronal function, and how these effects may reduce specific memory disturbances in aged subjects. The results of these studies demonstrate that the effects of combining choline and piracetam are quite different than those obtained with either drug alone and support the notion that in order to achieve substantial efficacy in aged subjects it may be necessary to reduce multiple, interactive neurochemical dysfunctions in the brain, or affect activity in more than one parameter of a deficient metabolic pathway.

Subtle cobalamin deficiency.

Carmel R.

No Abstract Available.

Prevention and treatment of Wernicke-Korsakoff syndrome.

Cook CC. Kent Institute of Medicine & Health Sciences, University of Kent at Canterbury, UK.

Alcohol Alcohol Suppl 2000 May-Jun;35 Suppl 1:19-20

Wernicke's encephalopathy (WE) is both common and associated with high morbidity and mortality and yet there is evidence that appropriate and effective prophylaxis and treatment are often not given. Effective treatment and prophylaxis may only be achieved by use of parenteral vitamin supplements, since oral supplements are not absorbed in significant amounts. Although there are rare anaphylactoid reactions associated with the use of parenteral thiamine preparations, the risks and consequences of inadequate prophylaxis and treatment, in appropriately targeted groups of patients, are far greater. It is therefore proposed that all in-patient alcohol withdrawal should be covered by prophylactic use of parenteral thiamine, that there should be a low threshold for making a presumptive diagnosis of WE, and that there is a need for guidelines to assist physicians in appropriate management of this common clinical problem.

Pregnenolone sulfate increases hippocampal acetylcholine release and spatial recognition.

Darnaudery M, Koehl M, Piazza PV, Le Moal M, Mayo W. Psychobiologie des Comportements Adaptatifs, INSERM U.259, Universite de Bordeaux 2, France.

Brain Res 2000 Jan 3;852(1):173-9

The pregnenolone sulfate is a neurosteroid with promnesic properties. Recently, a correlation between endogenous levels of pregnenolone sulfate in the hippocampus and performance in a spatial memory task has been reported in aged rats. Cholinergic transmission is known to modulate memory processes and to be altered with age. In the present experiment we investigated the effect of increasing doses of pregnenolone sulfate on hippocampal acetylcholine release. Our results show that intracerebroventricular administrations of this neurosteroid induced a dose-dependent increase in acetylcholine release. Administration of 12 and 48 nmol of pregnenolone sulfate induced a short lasting (20 min) enhancement of acetylcholine output with a maximum around 120% over baseline and the administration of 96 and 192 nmol doses induced a long-lasting (80 min) increase that peaked around 300% over baseline. In a second experiment we have observed that the 12 nmol dose enhanced spatial memory performance, whereas the 192 nmol dose was inefficient. These results are consistent with previous work suggesting that, a modest increase in acetylcholine release facilitates memory processes, while elevation beyond an optimal level is ineffective. Nevertheless, neurosteroids may be of value for reinforcing depressed cholinergic transmission in certain age-related memory disorders.

Ginkgo biloba extract (EGb 761) and CNS functions: basic studies and clinical applications.

DeFeudis FV, Drieu K. Institute for BioScience, 153 West Main Street, Westboro, MA 01581, USA. defeudi@prime-x.net

Curr Drug Targets 2000 Jul;1(1):25-58

The effects of EGb 761 on the CNS underlie one of its major therapeutic indications; i.e., individuals suffering from deteriorating cerebral mechanisms related to age-associated impairments of memory, attention and other cognitive functions. EGb 761 is currently used as symptomatic treatment for cerebral insufficiency that occurs during normal ageing or which may be due to degenerative dementia, vascular dementia or mixed forms of both, and for neurosensory disturbances. Depressive symptoms of patients with Alzheimer's disease (AD) and aged non-Alzheimer patients may also respond to treatment with EGb 761 since this extract has an "anti-stress" effect. Basic and clinical studies, conducted both in vitro and in vivo, support these beneficial neuroprotective effects of EGb 761. EGb 761 has several major actions; it enhances cognition, improves blood rheology and tissue metabolism, and opposes the detrimental effects of ischaemia. Several mechanisms of action are useful in explaining how EGb 761 benefits patients with AD and other age-related, neurodegenerative disorders. In animals, EGb 761 possesses antioxidant and free radical-scavenging activities, it reverses age-related losses in brain alpha 1-adrenergic, 5-HT1A and muscarinic receptors, protects against ischaemic neuronal death, preserves the function of the hippocampal mossy fiber system, increases hippocampal high-affinity choline uptake, inhibits the down-regulation of hippocampal glucocorticoid receptors, enhances neuronal plasticity, and counteracts the cognitive deficits that follow stress or traumatic brain injury. Identified chemical constituents of EGb 761 have been associated with certain actions. Both flavonoid and ginkgolide constituents are involved in the free radical-scavenging and antioxidant effects of EGb 761 which decrease tissue levels of reactive oxygen species (ROS) and inhibit membrane lipid peroxidation. Regarding EGb 761-induced regulation of cerebral glucose utilization, bilobalide increases the respiratory control ratio

of mitochondria by protecting against uncoupling of oxidative phosphorylation, thereby increasing ATP levels, a result that is supported by the finding that bilobalide increases the expression of the mitochondrial DNA-encoded COX III subunit of cytochrome oxidase. With regard to its "anti-stress" effect, EGb 761 acts via its ginkgolide constituents to decrease the expression of the peripheral benzodiazepine receptor (PBR) of the adrenal cortex.

The neurosteroid dehydroepiandrosterone sulfate (DHEAS) enhances hippocampal primed burst, but not long-term, potentiation.

Diamond DM, Branch BJ, Fleshner M. Department of Pharmacology, University of Colorado Health Sciences Center, Denver, USA. d.diamond@uchsc.edu

Neurosci Lett 1996 Jan 5;202(3):204-8

Dehydroepiandrosterone sulfate (DHEAS), which is synthesized in the brain and in the periphery, is known to affect the excitability of hippocampal neurons. However, its influence on electrophysiological plasticity has not been addressed. We have studied the effects of DHEAS on primed burst (PB) and long-term (LTP) potentiation, two electrophysiological models of memory. PB potentiation is a lasting increase in the amplitude of the CA1 population spike produced by minimal (threshold) electrical stimulation; LTP is produced by more extensive (supra-threshold) stimulation. Whereas intermediate doses (24 and 48 mg/kg, s.c.) of DHEAS given to rats enhanced PB potentiation, low (6 mg/kg) and high (96 mg/kg) doses were ineffective. LTP was not affected by any dose of DHEAS. The inverted-U relationship between DHEAS and PB potentiation is consistent with previous work demonstrating an inverted-U dose-dependent enhancement of memory by DHEAS. The present findings suggest that DHEAS could enhance memory by facilitating the induction of neural plasticity.

Ginkgo biloba extract: mechanisms and clinical indications.

Diamond BJ, Shiflett SC, Feiwel N, Matheis RJ, Noskin O, Richards JA, Schoenberger NE. Department of Research, Center for Research in Complementary and Alternative Medicine, Kessler Medical Rehabilitation Research and Education Corporation, West Orange, NJ 07052, USA.

Arch Phys Med Rehabil 2000 May;81(5):668-78

OBJECTIVE: Ginkgo biloba may have a role in treating impairments in memory, cognitive speed, activities of daily living (ADL), edema, inflammation, and free-radical toxicity associated with traumatic brain injury (TBI), Alzheimer's dementia, stroke, vasooclusive disorders, and aging. The purpose of this review is to provide a synthesis of the mechanisms of action, clinical indications, and safety of Ginkgo biloba extract.

DATA SOURCES: Empirical studies, reviews, chapters, and conference proceedings were identified in the following databases: Medline, the Research Council for Complementary Medicine based on the British Library database, and PsychInfo. Ginkgo biloba, EGb 761, Tanakan, Tebonin, Rokan, and LI 1370 were the principal index terms.

STUDY SELECTION AND DATA EXTRACTION: Controlled clinical studies with both positive and negative findings are included, in addition to animals studies illustrating mechanisms of activity.

DATA SYNTHESIS: Ginkgo has shown activity centrally and peripherally, affecting electrochemical, physiologic, neurologic, and vascular systems in animals and humans with few adverse side effects or drug interactions. Ginkgo shows promise in patients with dementia, normal aging, and cerebrovascular-related disorders. Clinical indications include memory, information processing, and ADL.

CONCLUSIONS: Ginkgo shows promise in treating some of the neurologic sequelae associated with Alzheimer's disease, TBI, stroke, normal aging, edema, tinnitus, and macular degeneration. Mechanisms of action may include antioxidant, neurotransmitter/receptor modulatory, and antiplatelet activating factor properties. While safe, caution is advised when recommending ginkgo to patients taking anticoagulants. Future studies should examine dose effects, component activity, mechanisms, and clinical applications.

Multicenter study with standardized extract of Ginkgo-Biloba EGB 761 in the treatment of memory alteration, vertigo and tinnitus.

Enrique Gomez, A

Invest Med Int. 1997; 24(2): 31-9. No Abstract Available

[A case of Wernicke-Korsakoff syndrome with dramatic improvement in consciousness immediately after intravenous infusion of thiamine]. [Article in Japanese]

Kikuchi A, Chida K, Misu T, Okita N, Nomura H, Konno H, Takase S, Takeda A, Itoyama Y. Department of Neurology, Kohnan Hospital, Sendai, Japan.

No To Shinkei 2000 Jan;52(1):59-63

A 68-year-old man was hospitalized on March 4, 1998 for disturbances in consciousness. In 1995, he had received proximal subtotal gastrectomy and reconstructive surgery of the jejunal interposition for gastric cancer. Thereafter he had been taking enough food without the habit of taking liquor. In October 1997, his short term memory was becoming gradually worse. On February 12, 1998, he suffered from numbness in the feet, and then dysphagia, unsteady gait, and diplopia developed gradually. On February 26, brain MRI showed no abnormalities. On March 3, he had a fever of 38.5 degrees C and his consciousness became unclear. Neurological examination revealed semi-coma, total ophthalmoplegia, and absence of doll's eye movement. Deep tendon reflexes were absent. The serum thiamine level was 9 ng/ml (normal range: 20-50). Brain MRI demonstrated symmetrical high intensity lesions in the periaqueductal area of the midbrain, dorsomedial nuclei of bilateral thalami, and vestibular nuclei. About 30 seconds after intravenous infusion of thiamine, his consciousness improved dramatically, but returned to semi-coma after about two minutes. Wernicke-Korsakoff syndrome usually occurs acutely. In the present case, however, the disease showed slow onset, chronic progression, and then rapid worsening after fever. Reconstructive surgery of the jejunal interposition might have caused the slow onset of Wernicke-Korsakoff syndrome, and fever might have facilitated the rapid progression of the disease. An immediate high concentration of thiamine modifies the kinetics of acetylcholine receptor ion channels, thereby maintaining wakefulness, and the level of consciousness may change dramatically.

Specificity of piracetam's anti-amnesic activity in three models of amnesia in the mouse.

Lenegre A; Chermat R; Avril I; Steru L; Porsolt RD I.T.E.M.-Labo, Kremlin-Bicetre, France.

Pharmacol Biochem Behav (United States) Mar 1988, 29 (3) p625-9

The effects of piracetam on the amnesias induced by scopolamine, diazepam and electroconvulsive shock (ECS) were studied in a passive avoidance procedure in the mouse and compared with the interactions of piracetam with the major behavioral effects of these treatments, namely scopolamine-induced hyperactivity, diazepam-induced release of punished behavior (Four Plates Test) and ECS-induced convulsions. Amnesia was induced by injecting scopolamine or diazepam (1 mg/kg, IP) 30 minutes before or applying ECS immediately after the first session (S1) of the passive avoidance task. Piracetam was studied at 3 doses (512, 1024 and 2048 mg/kg) administered PO 60 minutes before S1. Retention was measured 24 hours later (S2) in the absence of any treatment. Piracetam dose-dependently attenuated the memory deficits induced by the three amnesic treatments but did not affect either scopolamine-induced hyperactivity, diazepam-induced release of punished behavior or ECS-induced convulsions. These results point to the specificity of piracetam's anti-amnesic activity and, in particular, suggest that piracetam can suppress the memory disturbances induced by diazepam without affecting diazepam's anxiolytic activity. The test battery employed would therefore seem highly suitable for evaluating the potential nootropic activity of novel compounds.

Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or macrocytosis.

Lindenbaum J, Heaton EB, Savage DG, Brust JC, Garrett TJ, Podell ER, Marcell PD, Stabler SP, Allen RH. Department of Medicine, Columbia-Presbyterian Medical Center, New York, NY 10032.

N Engl J Med 1988 Jun 30;318(26):1720-8

Among 141 consecutive patients with neuro-psychiatric abnormalities due to cobalamin deficiency, we found that 40 (28 percent) had no anemia or macrocytosis. The hematocrit was normal in 34, the mean cell volume was normal in 25, and both tests were normal in 19. Characteristic features in such patients included paresthesia, sensory loss, ataxia, dementia, and psychiatric disorders; longstanding neurologic symptoms without anemia; normal white-cell and platelet counts and serum bilirubin and lactate dehydrogenase levels; and markedly elevated serum concentrations of methylmalonic acid and total homocysteine. Serum cobalamin levels were above 150 pmol per liter (200 pg per milliliter) in 2 patients, between 75 and 150 pmol per liter (100 and 200 pg per milliliter) in 16, and below 75 pmol per liter (100 pg per milliliter) in only 22. Except for one patient who died during the first week of treatment, every patient in this group benefited from cobalamin therapy. Responses included improvement in neuropsychiatric abnormalities (39 of 39), improvement (often within the normal range) in one or more hematologic findings (36 of 39), and a decrease of more than 50 percent in levels of serum methylmalonic acid, total homocysteine, or both (31 of 31). We conclude that neuropsychiatric disorders due to cobalamin deficiency occur commonly in the absence of anemia or an elevated mean cell volume and that measurements of serum methylmalonic acid and total homocysteine both before and after treatment are useful in the diagnosis of these patients.

EGG phosphatidylcholine combined with vitamin B12 improved memory impairment following lesioning of nucleus basalis in rats.

Masuda Y, Kokubu T, Yamashita M, Ikeda H, Inoue S. Q.P. Corporation, Department of Neuropsychiatry, Kochi Medical School, Tokyo, Japan.

Life Sci 1998;62(9):813-22

We investigated the effects of egg phosphatidylcholine (PC) combined with vitamin B12 on memory in the Morris water maze task, and on choline and acetylcholine (ACh) concentrations in the brain of rats. Animals with nucleus basalis Magnocellularis (NBM) lesion received intragastric administration of egg PC or vitamin B12, or both for 18 days. Memory acquisition and retention were remarkably impaired in NBM lesioned rats compared with in sham-operated control. NBM lesioned group had lower choline and ACh concentrations than control group in the frontal cortex. High dose of egg PC alone significantly increased choline concentration, but did not change ACh concentration in the frontal cortex. High dose of vitamin B12 alone did not change choline and ACh concentrations in the brain. Either egg PC or vitamin B12 did not improve memory acquisition and retention. However, low dose of egg PC combined with vitamin B12 significantly increased ACh concentration and improved memory acquisition and retention in the NBM lesioned rats. We concluded that egg PC combined with vitamin B12 improved the memory impairment of NBM lesioned rats through the action on the cholinergic neurons.

[Models for the study of memory and neurosteroids] [Article in French]

Mathis C, Meziane H, Ungerer A. Laboratoire d'Ethologie et de Neurobiologie, URA 1295 CNRS, Universite Louis Pasteur, Strasbourg, France. mathisc@currif.u-strasbg.fr

J Soc Biol 1999;193(3):299-306

The steroids dehydroepiandrosterone sulfate (DHEA-S) and pregnenolone sulfate (Preg-S) are naturally synthesized in the brain. They improve short term and long term memory performances in a variety of learning tasks and models of amnesia in rodents. DHEA-S and Preg-S modulate GABAergic and glutamatergic synaptic transmission through direct interactions with GABA-A, NMDA and/or sigma 1 membrane receptors. In addition, these two neurosteroids facilitate the release of acetylcholine and modulate synaptic plasticity phenomena in cerebral structures, such as the hippocampus, known to play a role in learning and memory processes. The possible links between these actions and the promnesic effects of DHEA-S and Preg-S are discussed in the present review.

Picamilon Enhances Blood Flow

Mirzoian RS; Gan'shina TS

Farmakol Toksikol (USSR) Jan-Feb 1989, 52 (1) p23-6

Picamilon, a sodium salt of N-nicotinoyl-gamma-aminobutyric acid, was shown to induce a significant increase of cerebral blood flow in conscious cats. Picamilon was found to inhibit neurogenic spasms of cerebral vessels, that were followed by suppression of tonic activity and reflectory discharges in sympathetic nerves. Picamilon led to restoration of the initial condition of cerebral hemodynamics disturbed by a previous administration of serotonin.

Effects of replacement dose of dehydroepiandrosterone in men and women of advancing age.

Morales AJ, Nolan JJ, Nelson JC, Yen SS. Department of Reproductive Medicine, University of California School of Medicine, La Jolla 92093-0802.

J Clin Endocrinol Metab 1994 Jun;78(6):1360-7

Aging in humans is accompanied by a progressive decline in the secretion of the adrenal androgens dehydroepiandrosterone (DHEA) and DHEA sulfate (DS), paralleling that of the GH-insulin-like growth factor-I (GH-IGF-I) axis. Although the functional relationship of the decline of the GH-IGF-I system and catabolism is recognized, the biological role of DHEA in human aging remains undefined. To test the hypothesis that the decline in DHEA may contribute to the shift from anabolism to catabolism associated with aging, we studied the effect of a replacement dose of DHEA in 13 men and 17 women, 40-70 yr of age. A randomized placebo-controlled cross-over trial of nightly oral DHEA administration (50 mg) of 6-month duration was conducted. During each treatment period, concentrations of androgens, lipids, apolipoproteins, IGF-I, IGF-binding protein-1 (IGFBP-1), IGFBP-3, insulin sensitivity, percent body fat, libido, and sense of well-being were measured. A subgroup of men (n = 8) and women (n = 5) underwent 24-h sampling at 20-min intervals for GH determinations. DHEA and DS serum levels were restored to those found in

young adults within 2 weeks of DHEA replacement and were sustained throughout the 3 months of the study. A 2-fold increase in serum levels of androgens (androstenedione, testosterone, and dihydrotestosterone) was observed in women, with only a small rise in androstenedione in men. There was no change in circulating levels of sex hormone-binding globulin, estrone, or estradiol in either gender. High density lipoprotein levels declined slightly in women, with no other lipid changes noted for either gender. Insulin sensitivity and percent body fat were unaltered. Although mean 24-h GH and IGFBP-3 levels were unchanged, serum IGF-I levels increased significantly, and IGFBP-1 decreased significantly for both genders, suggesting an increased bioavailability of IGF-I to target tissues. This was associated with a remarkable increase in perceived physical and psychological well-being for both men (67%) and women (84%) and no change in libido. In conclusion, restoring DHEA and DS to young adult levels in men and women of advancing age induced an increase in the bioavailability of IGF-I, as reflected by an increase in IGF-I and a decrease in IGFBP-1 levels. These observations together with improvement of physical and psychological well-being in both genders and the absence of side-effects constitute the first demonstration of novel effects of DHEA replacement in age-advanced men and women.

Antagonism of piracetam with proline in relation to amnestic effects

Ostrovskaja RU; Trofimov SS; Tsybina NM; Gudasheva TA; Skoldinov AP

Biull Eksp Biol Med (USSR) Mar 1985, 99 (3) p311-4

Based on the authors' previous data showing that the lipophilic cethyl group promotes the penetration of amino acids through the blood-brain barrier, proline cethyl ester was synthesized and studied as a neuropharmacological tool. The substance administered to rats systemically (intraperitoneally) was shown to be able to provoke a deep amnesia when tested by the conditioned avoidance performance. Piracetam abolished the amnestic effect of proline cethyl ester while sodium hydroxybutyrate administered in the dosage range provoking the nootropic effect did not change that amnesia. The data suggest that proline may be considered as one of the possible endogenous amnestic factors. The close structural similarity of the piracetam cyclic fragment to proline, which resulted in their competition, appears to be one of the reasons for piracetam antiamnestic activity.

The results of clinical study of the drug Picamilon (an analysis of some data of neurologic and psychiatric clinics)

A. P.huaichenko, R. P. Kruglikova-Lvova, The Pharmacological Committee of the Ministry of Health of USSR, 25, Kropotkinaky per., Moscow! NPO, "Vitamins," 14 A, Nauchny proezd, Moscow 117246, USSR

The analysis of results of Picamilon clinical investigation in 16 neurologic and psychiatric clinics on 984 patients with various diseases is presented. Picamilon efficiency and good tolerance were established. Picamilon was recommended by the Pharmacological Committee of the Ministry of Health of the USSR for application in medicine for insults therapy, for treatment of transient disorders and chronic insufficiency of blood circulation and also as a tranquillizer without the sedative component and myorelaxation; Picamilon is recommended for asthenic disorders within the limits of different psychical diseases and for treating depressions of old age. As a therapeutic and prophylactic remedy, Picamilon is recommended for rehabilitation of capacity for work and for increasing of stability towards physical and psychological burden. Picamilon is used in narcology in the period of abstinence.

[The effect of piracetam and nicergoline on conditioned-reflex memory under conditions of extreme exposure] [Article in Russian]

Pragina LL, Voronina TA, Inozemtsev AN, Kokaeva FF, Tushmalova NA.

Farmakol Toksikol 1990 May-Jun;53(3):8-10

The effects of nicergoline and piracetam on the learning of avoidance response and its restoration after disturbance produced by unexpected changes of the previously established cause-effect relations in experimental environment were studied. It was found that both drugs improve the learning, nicergoline being the most active in the initial period of training, meanwhile piracetam--beginning from the third day. The drugs prevent disturbance of the avoidance response but piracetam is more effective.

Dehydroepiandrosterone and the relationship with aging and memory: a possible link with protein kinase C functional machinery.

Racchi M, Govoni S, Solerte SB, Galli CL, Corsini E. Department of Experimental and Applied Pharmacology, University of Pavia, Viale Taramelli 14, 27100, Pavia, Italy. racchi@unipv.it

Brain Res Brain Res Rev 2001 Nov;37(1-3):287-93

A progressive decline of cognitive and memory functions, compared to the average young-life performance, characterizes brain

aging. The changes in performance may depend upon altered activity of neurotransmitters acting on attention and memory trace formation (acetylcholine, catecholamines, glutamate, for example) or the failure of the transduction mechanisms linked to receptor activation. One of the fundamental cellular changes associated with brain aging is the alteration of mechanisms involving the activity of the calcium-phospholipid-dependent protein kinase C (PKC). A crucial event for the activation of protein kinase C is its translocation from the cytosol to different intracellular sites and recent studies have demonstrated the key role played by several anchoring proteins in this mechanism. The defective activation of PKC-dependent pathways during aging is due to a defective mechanism of translocation of the kinase because of reduced levels of the major anchoring protein RACK-1 (receptor for activated C kinase). Pharmacological strategies aimed at the correction of age-associated memory deficits have been mostly focused on neurotransmitters using direct or indirect agonists. More recently, attention has been paid to the memory enhancing properties of some steroid hormones, namely 'neurosteroids'. Among these the activities of dehydroepiandrosterone (DHEA), pregnenolone (PREG) and their sulfates, have been extensively studied. These neuroactive steroids, can regulate neuronal function through their concurrent influence on transmitter-gated ion channels and gene expression. We addressed the possibility that DHEA, among other neurosteroids, could modulate directly the age-associated impairment of PKC signal transduction and provide experimental evidence that DHEA can revert the alteration of RACK-1 anchoring protein expression.

[Effects of piracetam during prolonged use in an experiment]

Rakhmankulova IKh; Garibova TL; Voronin KE; Tilekeeva UM; Voronina TA

Farmakol Toksikol (USSR) Jul-Aug 1985, 48 (4) p42-6

The spectrum of the pharmacological activity of piracetam administered for a long time was studied in experiments on mice and rats. It was established that administration of piracetam (300-400 mg/kg i. p.) for 10-42 days brought about potentiation of its anti-amnesic effect, retardation of the processes of extinction, an increase in the emotional responsiveness, and preservation of the tranquilizing effect with no side effects (sedative or myorelaxant). The characteristic feature of piracetam effect on the extinction is its ability to decelerate this process only after its prolonged administration. It is assumed that under prolonged administration of piracetam there takes place the formation of a new functional system ensuring the memory trace stabilization.

Aniracetam (Ro 13-5057) in the treatment of senile dementia of Alzheimer type (SDAT): results of a placebo controlled multicentre clinical study.

Senin U, Abate G, Fieschi C, Gori G, Guala A, Marini G, Villardita C, Parnetti L. Istituto di Gerontologia e Geriatria, Università di Perugia, Italy.

Eur Neuropsychopharmacol 1991 Dec;1(4):511-7

One hundred and nine elderly patients suffering from mild to moderate cognitive impairment fulfilling NINCDS-ADRDA criteria for probable dementia of the Alzheimer type were treated for 6 months with a new nootropic drug, aniracetam (Ro 13-5057) in a double-blind randomized study versus placebo. The two treatment groups were comparable at baseline for demographic and behavioural parameters and symptomatology. Patients underwent clinical, behavioural and psychometric evaluation every other month. The aniracetam group differed significantly from the placebo group by the end of the study and also showed a statistically significant improvement versus baseline in the psychobehavioural parameters, while in the placebo group a steady deterioration was observed. Tolerability to aniracetam was excellent.

The effect of 7-oxo-DHEA acetate on memory in young and old C57BL/6 mice.

Shi J, Schulze S, Lardy HA. Department of Biochemistry and Institute for Enzyme Research, University of Wisconsin-Madison, Madison, WI 53705-4098, USA.

Steroids 2000 Mar;65(3):124-9

7-Oxo-dehydroepiandrosterone, which can be formed from dehydroepiandrosterone (DHEA) by several mammalian tissues, is more effective than its parent steroid as an inducer of thermogenic enzymes when administered to rats. Using the Morris water maze procedure, we tested DHEA and its 7-oxo-derivative for their ability to reverse the memory abolition induced by scopolamine in young C57BL/6 mice, and for their effect on memory in old mice. A single dose of 7-oxo-DHEA-acetate at 24 mg/kg b.w. completely reversed the impairment caused by 1 mg of scopolamine per kg b.w. (< 0.001). DHEA (20 mg/kg) was also effective (< 0.01). In old mice given the same single doses followed by feeding 0.05% of the respective steroid in the diet, memory of the water maze training was retained through a four week test period in mice receiving 7-oxo-DHEA-acetate (< 0.05) but not in the control or DHEA-treated groups. When old mice were not tested until five weeks after being trained 7-oxo-DHEA exerted a slight, but statistically insignificant, improvement in memory retention. The possible effect of 7-oxo-DHEA in human memory problems deserves investigation.

Role of pregnenolone, dehydroepiandrosterone and their sulfate esters on learning and memory in cognitive aging.

Vallee M, Mayo W, Le Moal M. Institut F. Magendie-INSERM U259, Domaine de Carreire, Rue Camille Saint Saens, 33077, Cedex, Bordeaux, France. monique.vallee@bordeaux.inserm.fr

Brain Res Brain Res Rev 2001 Nov;37(1-3):301-12

Aging is a general process of functional decline which involves in particular a decline of cognitive abilities. However, the severity of this decline differs from one subject to another and inter-individual differences have been reported in humans and animals. These differences are of great interest especially as concerns investigation of the neurobiological factors involved in cognitive aging. Intensive pharmacological studies suggest that neurosteroids, which are steroids synthesized in the brain in an independent manner from peripheral steroid sources, could be involved in learning and memory processes. This review summarizes data in animals and humans in favor of a role of neurosteroids in cognitive aging. Studies in animals demonstrated that the neurosteroids pregnenolone (PREG) and dehydroepiandrosterone (DHEA), as sulfate derivatives (PREGS and DHEAS, respectively), display memory-enhancing properties in aged rodents. Moreover, it was recently shown that memory performance was correlated with PREGS levels in the hippocampus of 24-month-old rats. Human studies, however, have reported contradictory results. First, improvement of learning and memory dysfunction was found after DHEA administration to individuals with low DHEAS levels, but other studies failed to detect significant cognitive effects after DHEA administration. Second, cognitive dysfunctions have been associated with low DHEAS levels, high DHEAS levels, or high DHEA levels; while in other studies, no relationship was found. As future research perspectives, we propose the use of new methods of quantification of neurosteroids as a useful tool for understanding their respective role in improving learning and memory impairments associated with normal aging and/or with pathological aging, such as Alzheimer's disease.

Vasopressin and oxytocin. Their presence in the central nervous system and their functional significance in brain processes related to behaviour and memory.

van Wimersma Greidanus TB, Burbach JP, Veldhuis HD.

Acta Endocrinol Suppl (Copenh) 1986;276:85-94

Vasopressin and oxytocin exert pronounced effects on behaviour by a direct action on the brain. A single injection of vasopressin results in a long-term inhibition of extinction of a conditioned avoidance response suggesting that vasopressin triggers a long-term effect on the maintenance of a learned response, probably by facilitation of memory processes. In addition vasopressin improves passive avoidance behaviour, delays extinction of appetitive discrimination tasks, affects approach behaviour to an imprinting stimulus in ducklings, improves copulation rewarded behaviour of male rats in a T-maze, prevents or reverses amnesia induced by electroconvulsive shock, CO₂ inhalation, pentylentetrazol or puromycin. The majority of these effects of vasopressin in the various and sometimes relatively complex tasks may be explained by stimulatory influences of this neuropeptide on memory processes. Generally oxytocin exerts effects which are opposite to those of vasopressin and it has been suggested that oxytocin may be an amnesic neuropeptide. Various limbic system structures seem to act as the anatomical substrate for the behavioural effects of vasopressin. In particular the amygdala, the dentate gyrus of the hippocampal complex, the ventral hippocampus and the dorsal septum seem to be involved. Evidence has been obtained from experiments with homozygous diabetes insipidus rats and from experiments in which antisera were applied that endogenous vasopressin and oxytocin play a physiological role in brain processes related to memory. It appears that highly active fragments can be generated from vasopressin and experiments in which a fragment of vasopressin ([pGlu⁴, Cyt⁶]AVP-(4-8)) as well as an AVP-antagonist were used, reveal that the vasopressin receptors mediating the behavioural effects are situated in the brain and differ in specificity from the peripheral (blood pressure) vasopressin receptors. Generally the clinical data obtained so far with vasopressin treatment are in agreement with the results from animal experiments and they support the notion on the involvement of vasopressin in memory function. The sometimes reported conflicting results on vasopressin effects in certain patients (Korsakoff or Alzheimer) may have to do with the wide-spread pathology in these diseases.

Dehydroepiandrosterone (DHEA) treatment of depression.

Wolkowitz OM, Reus VI, Roberts E, Manfredi F, Chan T, Raum WJ, Ormiston S, Johnson R, Canick J, Brizendine L, Weingartner H. Department of Psychiatry, University of California, San Francisco, School of Medicine 94143-0984, USA.

Biol Psychiatry 1997 Feb 1;41(3):311-8

Dehydroepiandrosterone (DHEA) and its sulfate, DHEA-S, are plentiful adrenal steroid hormones that decrease with aging and may have significant neuropsychiatric effects. In this study, six middle-aged and elderly patients with major depression and low basal plasma DHEA f1p4or DHEA-S levels were openly administered DHEA (30-90 mg/d x 4 weeks) in doses sufficient to achieve circulating plasma levels observed in younger healthy individuals. Depression ratings, as well as aspects of memory performance significantly improved. One treatment-resistant patient received extended treatment with DHEA for 6 months: her depression ratings improved 48-72% and her semantic memory performance improved 63%. These measures returned to baseline after treatment

ended. In both studies, improvements in depression ratings and memory performance were directly related to increases in plasma levels of DHEA and DHEA-S and to increases in their ratios with plasma cortisol levels. These preliminary data suggest DHEA may have antidepressant and promemory effects and should encourage double-blind trials in depressed patients.

Ginkgo biloba leaf extract: review of biological actions and clinical applications.

Yoshikawa T, Naito Y, Kondo M. First Department of Medicine, Kyoto Prefectural University of Medicine, Japan. toshi@koto5.kpu-m.ac.jp

Antioxid Redox Signal 1999 Winter;1(4):469-80

The number of studies on Ginkgo biloba leaves is rapidly increasing. A variety of effects of Ginkgo biloba leaf extract (GBLE) have been identified. GBLE contains many different flavone glycosides and terpenoids. GBLE has an antioxidant action as a free radical scavenger, a relaxing effect on vascular walls, an antagonistic action on platelet-activating factor, an improving effect on blood flow or microcirculation, and a stimulating effect on neurotransmitters. Besides a direct scavenging action on active oxygen species, GBLE exerts an anti-inflammatory effect on inflammatory cells by suppressing the production of active oxygen and nitrogen species. GBLE inhibited the increase in the products of the oxidative decomposition low-density lipoprotein (LDL), reduced the cell death in various types of neuropathy, and prevented the oxidative damage to mitochondria, suggesting that GBLE exhibits beneficial effects on neuron degenerative diseases by preventing chronic oxidative damage. The study using a model of ischemia-reperfusion injury has also demonstrated the protective effect of GBLE on cardiac muscle and its antioxidative action in vivo. Favorable results have been obtained in double-blind, placebo-controlled, comparative trials of patients with memory disorders, obstructive arteriosclerosis, and dementia. We review the recent studies on GBLE with respect to its various pharmacological actions, such as a scavenging activity on free radicals and an inhibitory action on lipid peroxidation. GBLE shows a very strong scavenging action on free radicals, and is thus considered to be useful for the treatment of diseases related to the production of free radicals, such as ischemic heart disease, cerebral infarction, chronic inflammation, and aging.

SUGGESTED READING

Amnesia associated with electroconvulsive therapy: Progress in pharmacological prevention and treatment

Pollina D.A.; Calev A. Dr. D.A. Pollina, Department of Neurology, HSC T12-020, State University of New York, Stony Brook, NY 11794-8121 USA

CNS Drugs (New Zealand), 1997, 7/5 (381-387)

Pharmacological treatments have been used in an attempt to improve the memory dysfunction induced by electroconvulsive therapy (ECT). Despite promising results from animal studies, human studies report few successes. Piracetam and physostigmine have been reported to directly improve memory test scores. The use of caffeine and liothyronine (triiodothyronine; T3) has been reported to reduce the number of ECT treatments required to produce a therapeutic effect, thus indirectly reducing memory deficits. However, the majority of studies on pharmacological treatments report no success. Some studies suggest that reducing the dosage of medications regularly administered with ECT may reduce memory deficits. However, reducing these medications may not be fruitful as they are necessary to prevent the medical risks associated with ECT. Moreover, at the dosages used during ECT, these medications have not been consistently shown to adversely affect cognition. At present, better controlled studies are required to assist in the search for effective pharmaceutical agents to reduce the cognitive deficits associated with ECT.

Piracetam and fipexide prevent PTZ-kindling-provoked amnesia in rats

Genkova-Papazova M.G.; Lazarova-Bakarova M.B. M.G. Genkova-Papazova, Dept. of Experimental Pharmacology, Institute of Physiology, Bulgarian Academy of Sciences, Acad. G. Bonchev Str. bl. 23, 1113 Sofia Bulgaria

European Neuropsychopharmacology (Netherlands), 1996, 6/4 (285-290)

Deficit in active and inhibitory avoidance behaviour has been found in pentylenetetrazole (PTZ)-kindled rats. This supports the view that memory deficit is an integral part of epilepsy. In the present study we examined the effect of the nootropic drugs piracetam and fipexide on memory deficit induced by PTZ-kindling in shuttle-box- and step-down-trained rats. The retention in piracetam- and fipexide-treated animals was significantly improved compared to the kindled controls. The mechanisms of action of the two drugs are considered. The favourable effects of nootropic drugs in cases of amnesia provoked by PTZ-kindling might be of interest in clinical practice.

p-Hydroxybenzyl alcohol attenuates learning deficits in the inhibitory avoidance task: Involvement of serotonergic and dopaminergic systems

Chinese Journal of Physiology (Taiwan), 1996, 39/4 (265-273)

p-Hydroxybenzyl alcohol (HBA), an aglycone of gastrodin, is an active ingredient of *Gastrodia elata* B(LUME). In this study, we investigated the action of HBA on acquisition of an inhibitory avoidance response in rats and used piracetam as a positive control. The results indicated that scopolamine, a cholinergic receptor antagonist, injected before training impaired retention. HBA did not attenuate the scopolamine-induced impairment, but piracetam did. p-Chloroamphetamine, a serotonin releaser, injected before training impaired retention. HBA at 5 mg/kg and piracetam at 100 mg/kg could counteract the p-chloroamphetamine-induced deficit. Apomorphine, a dopaminergic receptor agonist, also impaired retention. HBA at 5 mg/kg and piracetam at 300 mg/kg could ameliorate the apomorphine-induced amnesia. The above results indicated that HBA, different from piracetam, can attenuate impairments induced by p-chloroamphetamine and apomorphine, but had no effect on impairment induced by scopolamine in an inhibitory avoidance task in rats. Such findings suggest that HBA may act through suppressing dopaminergic and serotonergic activities and thus improves learning.

Effect of mental stimulants on electroconvulsive shock-induced retrograde amnesia

Hoffmann W; Rostock A

Pharmazie (Germany, East) Dec 1983, 38 (12) p869-71

The effect of nootropics on the retrograde amnesia induced by electroshock was studied on a model of the active conditioned escape reaction (pole jumping). In untreated animals the daily application of electroshock for three days, immediately after the training, led to a significant retardation of the development of a conditioned escape reaction. The administration of nootropics influences the development of the retrograde amnesia to different extents, the treatment regimen (application of the drug only during the training and supplementary pretreatment before the first day of training; respectively) being of importance. The anti-amnesic effect of Piracetam (100 mg/kg, intraperitoneally) which is good also without pretreatment, may still be potentiated, especially on the fourth day of treatment, by an additional administration of the drug, beginning four days before the first day of treatment. In contrast to this, meclofenoxate hydrochloride (100 mg/kg, intraperitoneally) and pyritinol (100 mg/kg, intraperitoneally) produce a marked inhibition of the development of the retrograde amnesia only after pretreatment. Without pretreatment these drugs exert a slight or no effect. The marked anti-amnesic effect of methylglucaminorotate (225 mg/kg, intraperitoneally) and by an additional pretreatment. As to dihydroergotoxin (1 mg/kg; intraperitoneally), both treatment regimens were ineffective in the model used.

Hypoxia-induced amnesia in one-trial learning and pharmacological protection by piracetam.

Sara SJ; Lefevre D

Psychopharmacologia (Germany, West) 1972, 25 (1) p32-40

No Abstract Available

Pre-clinical evaluation of cognition enhancing drugs.

Schindler U Department of CNS Pharmacology, Cassella AG, Frankfurt, Federal Republic of Germany.

Prog Neuropsychopharmacol Biol Psychiatry (England) 1989, 13 Suppl pS99-115

1. The need of the treatment of cognitive impairment due to aging or dementia has led to the search for potential cognition enhancing drugs. The various compounds presently under development represent an alternative to the cholinomimetic therapy and include new chemical entities as well as piracetam and its newer analogs.
2. Recent results from pre-clinical evaluation of the effects on learning on memory are summarized. Emphasis is put on learning and memory experiments under normal and pathological conditions. Most of the nootropics attenuate experimental amnesias induced by scopolamine, cycloheximide, ECS, hemicholinium-3 or forebrain ischemia. These findings suggest that the nootropics may be influencing a common mechanism underlying the amnesias.
3. Biochemical data suggest a potential cholinergic neuronal activity of some of the piracetam analogs. They increase high-affinity choline uptake, and antagonize scopolamine and ECS-induced decreases in acetylcholine concentrations in the hippocampus. The mode of action of these and all other nootropic compounds, however, is still not known. 4. Despite the interesting results from learning and memory studies and from biochemical investigations, the clinical relevance of these results for amelioration of the

cognitive impairment in humans remains to be proven for most of the compounds. (51 Refs.)

Nootropic drugs and brain cholinergic mechanisms.

Pepeu G; Spignoli G Department of Preclinical and Clinical Pharmacology, University of Florence, Italy.

Prog Neuropsychopharmacol Biol Psychiatry (England) 1989, 13 Suppl pS77-88

1. This review has two aims: first, to marshal and discuss evidences demonstrating an interaction between nootropic drugs and brain cholinergic mechanisms; second, to define the relationship between the effects on cholinergic mechanisms and the cognitive process.
2. Direct or indirect evidences indicating an activation of cholinergic mechanisms exist for pyrrolidinone derivatives including piracetam, oxiracetam, aniracetam, pyroglutamic acid, tenilsetam and pramiracetam and for miscellaneous chemical structures such as vinpocetine, naloxone, ebitatide and phosphatidylserine. All these drugs prevent or revert scopolamine-induced disruption of several learning and memory paradigms in animal and man.
3. Some of the pyrrolidinone derivatives also prevent amnesia associated with inhibition of acetylcholine synthesis brought about by hemicholinium. Oxiracetam prevents the decrease in brain acetylcholine and amnesia caused by electroconvulsive shock. Oxiracetam, aniracetam and pyroglutamic acid prevent brain acetylcholine decrease and amnesia induced by scopolamine. Comparable bell-shaped dose-effect relationships result for both actions. Phosphatidylserine restores acetylcholine synthesis and conditioned responses in aging rats.
4. The mechanisms through which the action on cholinergic systems might take place, including stimulation of the high affinity choline uptake, are discussed. The information available are not yet sufficient to define at which steps of the cognitive process the action on cholinergic system plays a role and which are the influences of the changes in cholinergic function on other neurochemical mechanisms of learning and memory. (60 Refs.)

Systemic administration of ACTH or vasopressin reverses the amnestic effect of posttraining beta-endorphin or electroconvulsive shock but not that of intrahippocampal infusion of protein kinase inhibitors.

Izquierdo LA, Schroder N, Ardenghi P, Quevedo J, Netto CA, Medina JH, Izquierdo I. Departamento de Bioquimica, Instituto de Ciencias Basicas da Saude, UFRGS, Ramiro Barcellos, Brazil.

Neurobiol Learn Mem 1997 Sep;68(2):197-202

Retrograde amnesia was induced in rats trained in step-down inhibitory avoidance by four different treatments: an ip injection of beta-endorphin (1.0 microgram/kg), an electroconvulsive shock (ECS), an intrahippocampal infusion of the calcium/calmodulin protein kinase II inhibitor, KN62 (0.08 microgram/side), given 0 h after training, or an intrahippocampal infusion of the protein kinase A inhibitor, KT5720 (0.5 microgram/side), given 3 h after training. Pretest ip injections of ACTH (0.2 microgram/kg) or vasopressin (10.0 micrograms/kg), but not saline, reversed the amnesia caused by beta-endorphin and ECS but not that caused by the enzyme inhibitors. This suggests that the amnesia produced by intrahippocampal KN62 and KT5720 administration is stronger than that caused by ECS and beta-endorphin, possibly because the former interfere directly with specific steps of the core biochemical chain of events that underlies memory consolidation.

The effect of vasopressin analogue [d(CH₂)⁵(1),Tyr(Me)₂]AVP on memory process in rats with experimental amnesia.

Car H, Borawska M, Wisniewski K. Department of Pharmacology, Medical Academy, Bialystok, Poland.

Acta Neurobiol Exp (Warsz) 1995;55(3):207-11

We investigated the effect of a single 2 micrograms dose of vasopressin (AVP) analogue [d(CH₂)⁵(1),Tyr(Me)₂]AVP on the processes of retrieval of conditioned reflexes in rats with experimentally induced amnesia. The models used were: electroconvulsive shock (ECS) and hypoxia. It severely impaired the memory processes. The AVP analogue [d(CH₂)⁵(1),Tyr(Me)₂]AVP facilitated retrieval of passive avoidance in all animals.

disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.