THP et TIQ, MAGNESIUM :

Extraits et conclusions, partiellement traduits, de résumés d'articles

Sources : PubMed
Janvier 2007

(quelques articles parmi de très nombreux…)

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C.A.L.M.E.

RAPPEL : SALSOLINOL = autre nom des tetraisoquinolines (TIQ) (dont la THP)

Les traductions résumées en rouge me semblent les plus intéressantes en référence à notre expérience clinique

I – les Tetralsoquinolines et l'alcoolisme

Psychopharmacology (Berl). 1976 May 5;47(1):49-52. Links

Salsolinol differentially affects mice selected for sensitivity to alcohol.

- Church AC,
- Fuller JL,
- Dudek BC.

Results are interpreted as supporting the hypothesis that salsolinol-like substances may mediate some of the effects of alcohol on the central nervous system.

Le salsolinol affecte différemment les souris sélectionnées pour leur sensibilité à l'alcool

Les résultats sont interprétés comme soutenant l'hypothèse que les substances salsolinol-like peuvent servir de médiateurs dans certains effets de l'alcool sur le système nerveux central.

Science. 1977 Apr 29;196(4289):554-6. Links

Alcohol drinking: abnormal intake caused by tetrahydropapaveroline in brain.

- Myers RD,
- Melchior CL.

Tetrahydropapaveroline (THP), a dopamine-dopaldehyde condensation product, was delivered directly into the cerebral ventricle of rats automatically every 15 minutes for 12 days. The animals were given access to both water and ethylalcohol, the latter being presented in 12 concentrations from 3 to 30 percent. Within 3 to 6 days of the start of the infusion of THP, the rats, which normally rejected alcohol, drank alcohol solutions in increasingly excessive amounts; this was accompanied by symptoms that were similar to those of withdrawal and intoxication. These results provide evidence that an abnormal metabolite in the brain may produce the addictive state caused by alcoholic beverages.

Alcoolisation: absorption anormale causée par la THP dans le cerveau

La THP, produit de la condensation dopamine-dopaldéhyde, a été injectée directement dans le ventricule cérébral de rats automatiquement chaque 15 mn pendant 12 jours. Les animaux ont eu accès à la fois à de l'eau et de l'éthanol, le second étant présenté sous 12 concentrations de 3 à 30 %. Au bout de 3 à 6 jours, les rats, qui normalement rejetaient l'alcool, buvaient les solutions alcoolisées de façon croissante ; cela était accompagné de symptômes similaires à ceux du sevrage et de l'intoxication. Ces résultats prouvent à l'évidence qu'un métabolite anormal dans le cerveau peut produire un état addictif causé par les boissons alcooliques.

1: Alcohol Clin Exp Res. 1978 Apr;2(2):145-54. Links

Tetrahydroisoquinolines in the brain: the basis of an animal model of alcoholism.

- **Myers RD**.

Quite surprisingly, the direct introduction of THP into the brain induces a remarkable shift in voluntary alcohol intake... Even as much as 6 month later, with no further infusions of THP, the remarkable voluntary selection of alcohol did not abate.

TIQs dans le cerveau: la base d'un modèle animal de l'alcoolisme

De manière surprenante, l'introduction directe de THP dans le cerveau induit un remarquable changement dans l'absorption volontaire d'alcool… Même après plus de 6 mois, sans autre perfusion de THP, le remarquable choix volontaire d'alcool n'a pas diminué.

1: Res Commun Chem Pathol Pharmacol. 1980 Jan;27(1):3-16. Links

Opiate receptor binding and analgesic effects of the tetrahydroisoquinolines salsolinol and tetrahydropapaveroline.

- **Fertel RH**,
- **Greenwald JE**,
- **Schwarz R**,
- **Wong L**,
- **Bianchine J**.

Salosolinol and tetrahydropapaveroline bind to opiate receptors in rat brain with affinities of 6.2 and 1.95 x 10(-5)M respectively. Their ability to displace 3H-naloxone is decreased about 4-fold by 100 mM sodium ion. Both of these agents have antinociceptive effects when given to rats intraventricularly. Their potency is comparable to the enkephalins, and their effect is blocked by naloxone.

Liens entre le récepteur opiacé et les effets analgésiques du salsolinol TIQ et la THP

(…) Ces deux agents ont des effets antinociceptifs quand on les donne aux rats au niveau intraventriculaire. Leur pouvoir est comparable aux enképhalines, et leur effet est bloqué par la naloxone.

Pharmacol Biochem Behav. 1980 Aug;13(2):265-81. Links

A critical evaluation of tetrahydroisoquinoline induced ethanol preference in rats.

- **Duncan C**,
- **Deitrich RA**.

Generally we have confirmed that rats of the Sprague-Dawley and Long-Evans strains do increase their alcohol intake in response to infused THP or salsolinol and that the effect is long lasting, up to 10 months.

We conclude that these compounds do shift these animals preference for alcohol relatively permanently, but not to the point of gross intoxication nor into the highly aversive range of alcohol concentration. We cannot confirm the reports that salsolinol or THP produce withdrawal symptoms when infused.

Une évaluation critique du TIQ induisant une préférence éthylique chez les rats

(…) Nous concluons que ces composés changent effectivement la préférence de ces animaux pour l'alcool de manière relativement permanente, mais pas au point d'une grosse intoxication ni dans la portée hautement aversive de la concentration en alcool. Nous ne pouvons confirmer les rapports selon lesquels le salsolinol ou la THP déclenchent des symptômes de sevrage quand ils sont perfusés.

Pharmacol Biochem Behav. 1982 Jun;16(6):995-1000. Links

Alcohol drinking induced in the monkey by tetrahydropapaveroline (THP) infused into the cerebral ventricle.

- Myers RD,
- McCaleb ML,
- Ruwe WD.

Overall, these results with the primate corroborate earlier findings in the rat of abnormal alcohol intake produced by centrally infused THP. They further support the theory that amine-aldehyde metabolites, if present in certain concentrations in the brain, may constitute a causal neurochemical factor in the addictive or otherwise immoderate drinking of alcohol.

Consommation d'alcool induite chez le singe par injection de THP dans le ventricule cérébral

Ces résultats avec les primates corroborent les premières découvertes sur la consommation anormale d'alcool chez le rat produite par la perfusion centrale de THP. De plus, ils soutiennent la théorie selon laquelle les métabolites amine-aldéhyde, s'ils sont présents à certaines concentrations dans le cerveau, peuvent constituer un facteur neurochimique causal dans les consommations addictives ou immodérées d'alcool.

Pharmacol Biochem Behav. 1982 May;16(5):827-36. Links

Naloxone alters alcohol drinking induced in the rat by tetrahydropapaveroline (THP) infused ICV.

- Myers RD,
- Critcher EC.

These results further support the suggestion of a possible opiate receptor link in the pathogenesis and maintenance of aberrant drinking of alcohol, the mechanism of which may involve the endogenous action of an amine-aldehyde condensation product in the brain.

La naloxone altère l'alcoolisation induite chez le rat par l'injection ICV de THP

Ces résultats soutiennent la suggestion d'un lien possible avec le récepteur opiacé dans la pathogénie et le maintien d'une consommation aberrante d'alcool, dont le mécanisme inclut l'action endogène d'un produit de condensation amine-aldéhyde dans le cerveau.

Acta Pharmacol Toxicol (Copenh). 1984 Nov;55(5):380-5. Links

Binding of beta-carbolines and tetrahydroisoquinolines by opiate receptors of the delta-type.

- Airaksinen MM,
- Saano V,
- Steidel E,
- Juvonen H,
- Huhtikangas A,
- Gynther J.

The Na dependence suggests that BC's and salsolinol are antagonists or partial agonists of opioids.

Acetaldehyde and its condensation products as markers in alcoholism.

- Collins MA.

Department of Biochemistry and Biophysics, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois 60153.

Several studies show that recently abstaining alcoholics generate higher circulating levels of acetaldehyde than nonalcoholics following ethanol administration. It is conceivable that levels of stable adducts (tetrahydroisoquinolines and tetrahydro-beta-carbolines) derived from acetaldehyde condensations with biogenic amines also might be increased in alcoholics consuming ethanol, thus serving in body fluids as chemical markers that are more persistent than acetaldehyde itself.

Condensation product measurements are complicated not only by artifacts (formation during analyses), but by other inherent problems. Products of interest often are constituents of diets and alcoholic beverages. For this and perhaps endogenous metabolic reasons, traces of condensation products are normally excreted by nondrinking individuals. Furthermore, the assays require high sensitivity and specificity and are not easily adapted to routine use. Thus, although several condensation products have initial appeal as clinical or pathological indicators in chronic alcoholism, thorough and statistically sound studies are needed before conclusions can be reached concerning any particular biogenic amine-derived product.

Acetaldéhyde et ses produits de condensation comme marqueurs de l'alcoolisme

(…) Il est concevable que les niveaux de TIQ et de THBetaCarboline dérivés des condensations d'acetaldéhyde avec les amines biogéniques puissent aussi être augmentés chez les alcooliques consommant de l'ethanol, servant ainsi dans les fluides corporels de marqueurs chimiques plus persistants que l'acetaldéhyde lui-même. (…) des traces de ces produits de condensation sont normalement excrétés par les personnes non-consommatrices d'alcool. De plus, les essais nécessitent une haute sensibilité et une haute spécificité, et ne sont pas aisément adaptés à un usage de routine.

Alcohol Clin Exp Res. 1989 Apr;13(2):155-63. Links

Elevation of plasma salsolinol sulfate in chronic alcoholics as compared to nonalcoholics.

- **Faraj BA**,
- **Camp VM**,
- **Davis DC**,
- **Lenton JD**,
- **Kutner M**.

Elevation of plasma salsolinol sulfate reported here may be interpreted as a reflection of abnormalities in oxidative metabolism of dopamine, metabolically derived acetaldehyde, and/or biological carbonyls in chronic alcoholics.

J Neurochem. 1990 Nov;55(5):1507-14. Links

Brain and plasma tetrahydroisoquinolines in rats: effects of chronic ethanol intake and diet.

- Collins MA,
- Ung-Chhun N,
- Cheng BY,
- Pronger D.

Brain concentrations of salsolinol (SAL), a simple tetrahydroisoquinoline (sTIQ) condensation product of dopamine (DA) and acetaldehyde, are reported to increase in chow-fed rats drinking ethanol/H2O ad libitum.

Overall, the data indicate that elevations in endogenous sTIQ concentrations due to prolonged ethanol intake depend on the brain region, duration of intake, and even associated dietary constituents. In that regard, the higher striatal SAL concentrations in rats drinking ethanol ad libitum could have been facilitated by DOPA and perhaps SAL consumed in lab chow.

TIQs dans le cerveau et le plasma des rats : effets de l'alcoolisation chronique et du régime alimentaire

(…) les données indiquent que les quantités de concentrations en TIQs endogènes dues à une consommation prolongée d'alcool dépendent de la région du cerveau, la durée de l'alcoolisation, et même des constituants associés du régime alimentaire.

Alcohol. 1990 Sep-Oct;7(5):449-59. Links

Anatomical "circuitry" in the brain mediating alcohol drinking revealed by THP-reactive sites in the limbic system.

- Myers RD.

Department of Pharmacology, School of Medicine, East Carolina University, Greenville, NC 27858-4354.

The involvement of aldehyde adducts in the etiology of alcoholism continues to be supported by a number of experimental findings. These metabolites are synthesized endogenously from a condensation reaction of a biogenic aldehyde with a catechol- or indole-amine and act in the brain to augment or suppress the drinking of ethyl alcohol. When given by the intracerebroventricular route in an animal which does not prefer alcohol, certain tetrahydro-isoquinolines and beta-carbolines can augment significantly the voluntary intake of alcohol even in aversive concentrations. This paper describes the historical background and current status of the "Multiple Metabolite" theory of alcoholism. The recent identification of anatomical structures in the limbic-midbrain, limbic-forebrain of

the Sprague-Dawley rat, which mediate changes in the intake of alcohol induced by tetrahydropapaveroline (THP) is also described. When injected in a low dose of 25 ng in a specific site, over a 3-day period, THP induces persistent increases in the intake of alcohol even in aversive concentrations. These THP-reactive sites comprise the substantia nigra, reticular formation, medial lemniscus, zona incerta, medial forebrain bundle, nucleus accumbens, olfactory tubercle, lateral septal nucleus, preoptic area, stria terminalis, and rostral hippocampus. A higher dose of 250 ng THP microinjected at homologous loci tends to inhibit the rat's self-selection of alcohol or exert no effect on drinking. Morphological mapping of histologically identified sites sensitive to THP revealed a distinct "circuitry" of neuronal structures overlapping both dopaminergic and enkephalinergic pathways. This "circuit" extends from the tegmental-nigral area of the midbrain rostrally to structures within the limbic-forebrain. When a THP-reactive structure, the N. accumbens, was lesioned by either of two neurotoxins, 6-hydroxydopamine or 5.7-dihydroxytryptamine, the rats' preference for alcohol increased sharply. This suggests that impairment of transmitter release, denervation supersensitivity or other perturbation of receptor function within this and other structures play a part in the aberrant drinking of alcohol. It is envisaged that a dopamine-enkephalin link underlies the mechanism for the onset, maintenance and permanency of alcohol preference generated by an aldehyde adduct. Finally, the "Two-Channel, Brain Metabolite" theory of alcoholism proposes that the transitory presence of an endogenously formed aldehyde adduct within cells of the brain causes a permanent perturbation of normal receptor processes and transmitter activity within synapses of specific structures of the limbic system. This theory thus explains the nature of the rewarding properties of alcohol as well as its complex addictive liability which is physiologically irreversible.

Le “circuit” anatomique qui dans le cerveau sert de médiateur à la consommation d’alcool, révélé par les sites réactifs à la THP dans le système limbique

(…) Quand on les donne, par voie intracerebroventiculaire, à un animal qui n’aime pas l’alcool, certains TIQs et beta-carbolines peuvent augmenter de manière significative l’absorption volontaire d’alcool même à des doses aversives. (….) Une cartographie morphologique des sites histologiquement identifiés qui sont sensibles à la THP, a révélé un « circuit » distinct de structures neuronales s’imbriquant à la fois sur les voies dopaminergiques et enképohalinergiques. (…) Il est envisagé qu’un lien dopamine-enképhaline sous-tend le mécanisme depuis son début, le maintien et la permanence de la préférence pour l’alcool générés par un dérivé de l’aldéhyde. Au bout du compte, la théorie de l’alcoolisme « double canal, métabolite cérébral » propose que la présence transitoire d’un dérivé endogène d’aldéhyde parmi les cellules du cerveau cause une perturbation permanente des processus permanents du récepteur normal et de l’activité des transmetteurs parmi les synapses de structures spécifiques du système limbique. Cette théorie explique ainsi la nature des propriétés de récompense de l’alcool autant que la responsabilité complexe dans l’addiction qui est physiologiquement irréversible.

Functional alterations in cerebral GABAA receptor complex associated with formation of alcohol dependence: analysis using GABA-dependent 36Cl- influx into neuronal membrane vesicles.

- Kuriyama K,
- Ueha T.

These results suggest that the observed functional deteriorations at cerebral GABAA receptors such as the decrease of GABA-dependent 36Cl- influx and the disappearance of the activating effects of ethanol, flunitrazepam and salsolinol on the influx may contribute to the preparation of the exhibition of ethanol withdrawal signs and/or the establishment of functional tolerance to alcohol, but are not directly related to the exhibition of alcohol withdrawal signs.

Alcohol. 1995 Jul-Aug;12(4):309-15. Links

Determination of (R)- and (S)-salsolinol sulfate and dopamine sulfate levels in plasma of nonalcoholics and alcoholics.

- Rommelspacher H,
- Sllstrom Baum S,
- Dufeu P,
- Schmidt LG.

Patients with alcoholic parents had lowered (R)-SAL and (S)-SAL levels compared with family history negative alcoholics, suggesting genetic association of disturbance of the SAL biosynthesis and alcoholism. Among the personality traits, suicidality was linked with low (R)-SAL and (S)-SAL concentrations in contrast to novelty seeking, impulsivity, and harm avoidance scores. The scores on the self-rating anxiety scale correlated positive with (R)-SAL. These findings suggest trait marker characteristics of salsolinol.

Détermination des niveaux de R et S sulfate de salsolinol et de sulfate de dopamine dans le plasma des non-alcooliques et des alcooliques

Les patients avec des parents alcooliques ont des niveaux abaissés de SAL comparés à ceux qui ont une histoire familiale négative, ce qui suggère une association génétique entre la perturbation de la biosynthèse du SAL et l'alcoolisme.

Alcohol. 1999 May;18(1):83-90. Links

Tetrahydropapaveroline injected in the ventral tegmental area shifts dopamine efflux differentially in the shell and core of nucleus accumbens in high-ethanol-preferring (HEP) rats.

- Myers RD,
- Robinson DE.

Since the 1970s tetrahydropapaveroline (THP) and other tetrahydroisoquinoline alkaloids have been implicated in the etiology of alcoholism. When injected into the cerebral ventricle or at specific sites in the mesolimbic system such as the ventral tegmental area (VTA), THP evokes spontaneous and intense intake of alcohol in the nondrinking animal. Further, THP evokes the extracellular efflux of dopamine in the nucleus accumbens (NAC), which comprises, in part, the postulated alcohol drinking "circuit" of neurons.

These results demonstrate that the presence of THP in the VTA alters directly the function of the pathway of mesolimbic neurons generally and the dopaminergic system specifically. That such a perturbation could account for the induction of alcohol preference is proposed in relation to a reinforcing mechanism involving opioidergic and dopaminergic elements.

Addict Biol. 2002 Oct;7(4):403-7. Links

Assay of salsolinol in peripheral blood mononuclear cells of alcoholics and healthy subjects by gas chromatography-mass spectrometry.

- Haber H,
- Jahn H,
- Ehrenreich H,
- Melzig MF.

After 13 weeks of abstinence a further significant decrease of SAL levels could be seen in the lymphocytes of alcoholics. The findings of this study support the theory that salsolinol might be a trait marker in alcoholism.

Dosage du salsolinol dans les cellules mononucléaires du sang périphérique des alcooliques et des sujets sains par la spectrométrie…

Après 13 semaines d'abstinence une diminution significative des niveaux de SAL peuvent être visibles dans les lymphocytes des alcooliques. Les découvertes de cette étude soutiennent la théorie que le salsolinol pourrait être un marqueur dans l'alcoolisme.

Alcohol Clin Exp Res. 2003 Mar;27(3):440-9. Links

Salsolinol produces reinforcing effects in the nucleus accumbens shell of alcohol-preferring (P) rats.

- Rodd ZA,
- Bell RL,
- Zhang Y,
- Goldstein A,
- Zaffaroni A,
- McBride WJ,
- Li TK.

SAL is reinforcing in the nucleus accumbens shell of P rats at concentrations that are pharmacologically possible, and these reinforcing actions are mediated in part by D2/D3-like receptors.

Neurotox Res. 2003;5(1-2):147-55. Links

A possible physiological role for cerebral tetrahydroisoquinolines.

- Vetulani J,
- Antkiewicz-Michaluk L,
- Nalepa I,
- Sansone M.

The results indicate that salsolinol and TIQ act as specific antagonists of agonistic conformation of dopamine receptors, and owing to that may play a role of endogenous feed-back regulators of the dopaminergic system. Those properties make tetrahydroisoquinolines potential antidopaminergic drugs devoid of extrapyramidal effects, with possible application in substance addiction disorder as anti-craving agents.

Un rôle physiologique possible des TIQs cérébraux

Ces résultats indiquent que le SAL et le TIQ agissent comme des antagonistes spécifiques de la conformation agonistique des récepteurs dopaminergiques, et grâce à cela jouent un rôle de régulateur des feed-back endogènes du système dopaminergique. Ces propriétés placent les TIQs comme des médicaments potentiellement antidopaminergiques dépourvus d'effets extrapyramidaux, avec une application possible dans les troubles d'addiction à une substance comme des agents anti-désir (craving).

II – Le Magnésium et l'alcoolisme

Clin Calcium. 2004 Aug;14(8):76-80

[Role of magnesium ions on the regulation of NMDA receptor-- a pharmacopathology of memantine]

[Article in Japanese]

- **Kato T**.

Yokohama City University Graduate School of Integrated Science, Laboratories of Molecular Recognition and Information Science.

Magnesium ion blocks the ion channel of the NMDA receptor at a stable condition. The ion channel competes with the binding site of the noncompetitive antagonists phencyclidine (PCP) and MK-801, which prevent a brain impairment due to the ischemia and so on. The binding ability of these antagonists is strong, an exchange with the magnesium ion is not easy, then the side effect of the schizophrenia-like behavior is caused. Recently, memantine can be used as a therapeutic drug of the moderate-to-severe Alzheimer's disease. Memantine is the noncompetitive antagonist, too, then those development details and a difference from MK-801 were explained.

Rôle du magnésium dans la régulation du récepteur NMDA - une pharmacologie de la mémantine

L'ion magnésium bloque le canal ionique du récepteur NMDA en une condition stable.

Eur J Pharmacol. 2007 Jan 12;554(2-3):123-7. Epub 2006 Oct 19. ELSEVIER FULL-TEXT ARTICLE Links

Modulation of cholestasis-induced antinociception in rats by two NMDA receptor antagonists: MK-801 and magnesium sulfate.

- Hasanein P,
- Parviz M,
- Keshavarz M,
- Javanmardi K,
- Allahtavakoli M,
- Ghaseminejad M.

Department of Physiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran; Department of Biology, Bu-Ali Sina University, Hamadan, Iran.

Acute cholestasis is associated with increased activity of the endogenous opioid system that results to changes including analgesia. N-methyl-d-aspartate (NMDA) receptors are involved in the nociceptive pathway and play a major role in the development of morphine induced analgesia. The magnesium acts as a non-competitive NMDA receptor antagonist by blocking the NMDA receptor channel. Considering the reported antinociceptive effect of magnesium sulfate as a NMDA receptor antagonist and the existence of close functional links between NMDA receptor antagonists and magnesium with the opioid system, we studied the effect of acute and chronic administration of MK-801 as a NMDA antagonist and magnesium sulfate on modulation of nociception in an experimental model of elevated endogenous opioid tone, acute cholestasis, using the tail-flick paradigm. Cholestasis was induced by ligation of the main bile duct using two ligatures and then transsection of the duct at the midpoint between them. A significant increase ($P<0.001$) in nociception threshold was observed in bile duct ligated rats compared to unoperated and sham-operated animals. In acute treatment, MK-801 (0.1 mg/kg, b.i.d), but not magnesium (150 mg/kg magnesium sulfate, i.e. 30 mg/kg of Mg(+2), i.p., b.i.d.) increased antinociception in cholestatic rats compared to saline treated cholestatics ($P<0.05$). In chronic treatment, administration of MK-801 or magnesium sulfate for 7 consecutive days, increased tail-flick latency ($P<0.05$, $P<0.01$) in cholestatic animals compared to saline treated cholestatics. These data showed that NMDA receptor pathway is involved in modulation of cholestasis-induced antinociception in rats and that repeated dosages of magnesium sulfate similar to MK-801 is able to modulate nociception in cholestasis.

Modulation de l'anti-nociception induite par la cholestase chez le rat au moyen de deux antagonistes du récepteur NMDA : MK-801 et Sulfate de magnesium

(…) Considérant les effets antinociceptifs rapportés du sulfate de magnésium comme antagoniste du récepteur NMDA et l'existence d'un lien fonctionnel étroit entre les antagonistes du récepteur NMDA et du magnésium avec le système opioïde…
(…) Ces données montrent que la voie du récepteur NMDA est impliquée dans la modulation de l'anti-nociception induite par la cholestase chez le rat et que des doses répétées de sulfate de magnésium similaires au MK-801 peuvent moduler la nociception dans la cholestase.

Alcohol Alcohol. 1993 Nov;28(6):639-47.

Modulation of alcohol preference by NMDA antagonists in male rats.

- Lamblin F,
- Deuceuninck D,
- De Witte P.

Universite Catholique de Louvain, Lab. Psychobiologie, Belgium.

Chronic alcoholization by alcohol inhalation was used to study the properties of magnesium, a non-competitive NMDA receptor antagonist, and CGP 39551, a competitive NMDA receptor antagonist, on behavioural dependence as estimated by the free-choice paradigm [alcohol 10% (v/v) vs. water], on the hypermotility after alcohol withdrawal, and finally on the cortical vascularization. The first experimental group received the drugs per os during the whole alcoholization period. Magnesium (20 mg/kg/day) decreased the alcohol dependence while CGP 39551 (5 and 10 mg/kg/day) increased, in a dose-dependent manner, the dependence to alcohol. A second group of animals received the same drugs at the same dosages, not simultaneously during chronic alcoholization, but immediately after alcoholization in one shot i.p. injection. In this case, rats receiving 5 mg/kg CGP 39551 never showed any dependence towards alcohol, while 10 mg/kg CGP 39551 or 20 mg/kg magnesium prolonged the number of days of alcohol dependence. These results thus indicate the close interaction between NMDA receptor function and dependence for alcohol. Magnesium had no effects on hypermotility, while CGP 39551-treated animals presented a decrease in the hypermotility observed after alcohol withdrawal. Neither drug affected the hypervascularization accompanying the chronic alcoholization.

Modulation de la préférence à l'alcool par des antagonistes NMDA chez les rats mâles

(…) Le magnésium (20mg/kg/jour) réduisait la dépendance à l'alcool, alors que le CGP l'augmentait. (…) Ces résultats indiquent l'étroite interaction entre le fonctionnement du récepteur NMDA et la dépendance à l'alcool. Le magnésium n'a eu aucun effet sur l'hypermotilité …

Alcohol Clin Exp Res. 1994 Oct;18(5):1069-75. Links

Effects of ethanol on NMDA receptors in brain: possibilities for Mg(2+)-ethanol interactions.

- Michaelis ML,
- Michaelis EK.

Department of Pharmacology and Toxicology, University of Kansas, Lawrence 66045.

The major excitatory neurotransmitter in the CNS is L-glutamate, and one of the subtypes of L-glutamate receptors, the N-methyl-D-aspartate (NMDA) subtype, has been found to be quite sensitive to inhibition by low concentrations of ethanol (5-50 mM). The NMDA receptor-ion channels are unique in that they exhibit a voltage-dependent blockade by physiological concentrations of Mg2+, a blockade that is relieved as the cell membrane is depolarized. Several lines of evidence also suggest that the activity of this receptor-channel complex may be regulated through a high-affinity Mg2+ site, which is distinct from the channel-blocking site and could even be located on the extracellular domain of the protein. This high-affinity Mg2+ site has been shown to increase the binding of N-[1-(2-thienyl) cyclohexyl]piperidine within the ion channel, as well as the binding of competitive antagonist such as 3-(+/-)-carboxypiperazine-4-yl)-[1,2]-propyl-1-phosphonic acid and the receptor coactivator glycine. The relationship between the acute effects of ethanol on receptor activation and the regulatory properties of Mg2+ is not yet known, although the hypomagnesemia that occurs in chronic alcoholism could certainly have implications for receptor function. A significant amount of molecular characterization of the multiple isoforms of the NMDA receptor-ion channel will be required before the role of Mg2+ can be clarified and any relationship between Mg2+ regulation and ethanol inhibition established.

Effets de l'éthanol sur les récepteurs NMDA dans le cerveau: possibilités d'interactions entre le magnésium (2+) et l'éthanol

(…) Les canaux ioniques du récepteur NMDA sont uniques en ceci qu'ils montrent un blocage voltage-dépendant par des concentrations physiologiques de Mg2+, blocage constaté pendant que la membrane de la cellule est dépolarisée. (…) La relation entre les effets aigus de l'éthanol sur l'activation du récepteur et les propriétés de régulation du Mg2+ n'est pas encore connue, quoique l'hypomagnésémie qui se produit dans l'alcoolisme chronique pourrait certainement avoir des implications pour le fonctionnement du récepteur. Une quantité signifiante de caractérisation des multiples isoformes du canal ionique du récepteur NMDA doit être requise avant que le rôle du Mg2+ puisse être clarifié et qu'une relation entre une régulation par le Mg2+et une inhibition de l'éthanol soit établie.

Br J Psychiatry. 1990 Oct;157:491-9. Links

Comment in:
Br J Psychiatry. 1991 Jan;158:133.

Overexcitement and disinhibition. Dynamic neurotransmitter interactions in alcohol withdrawal.

- **Glue P**,
- **Nutt D**.

Reckitt and Colman Psychopharmacology Unit, Department of Pharmacology, Medical School, Bristol.

In alcohol withdrawal, abnormalities occur in a number of neurotransmitter systems: there is reduced inhibitory function, and increased activity of excitatory systems. The former, indicated by reduced GABA and alpha-2-adrenoceptor activity, acts in conjunction with, and is exacerbated by, the latter, which itself may be due to the potentiation of NMDA activity by depletion of magnesium, and overactivity of catecholaminergic and CRF neurones. These dysfunctions produce immediate effects and may also contribute to the long-term changes in brain excitability by a kindling-like process. It is possible that early and active treatment may oppose this process. Present strategies for treatment of alcohol withdrawal enhance GABA and alpha-2 inhibitory, or reduce excitatory, mechanisms. Future possibilities include the use of CRF and/or NMDA antagonists.

Surexcitation et désinhibition. Interactions dynamiques des neurotransmetteurs dans le sevrage alcoolique.

Dans le sevrage alcoolique, des anomalies se produisent dans plusieurs systèmes de neurotransmetteurs : il y a une réduction du fonctionnement inhibiteur, et une augmentation de l'activité des systèmes excitateurs. Le premier, indiqué par la réduction d'activité du GABA et de l'alpha-2-adrenorécepteur, agit en conjonction avec, et est exacerbé par, le second, qui lui-même peut-être due à la potentialisation de l'activité NMDA par déficience en magnésium, et la suractivité des neurones catécholaminergiques et du CRF (facteur déclenchant la corticostimuline). Ces dysfonctionnements produisent des effets immédiats et peuvent aussi contribuer aux changements à long terme de l'excitabilité cérébrale par un processus d'embrasement. Il est possible qu'un traitement précoce et actif puisse s'opposer à ce processus. Les stratégies actuelles de traitement de sevrage alcoolique réhaussent les mécanismes d'inhibition du GABA et de l'alpha-2, ou réduisent les mécanismes d'excitation. De futures possibilités incluent l'utilisation d'antagonistes du CRF et/ou du NMDA.

Psychiatr Pol. 2005 Sep-Oct;39(5):911-20. Links

[The role of copper and magnesium in the pathogenesis and treatment of affective disorders]

[Article in Polish]

- Siwek M,
- Wrobel A,
- Dudek D,
- Nowak G,
- Zieba A.

Klinika Psychiatrii Doroslych CM UJ.

Magnesium and copper are important modulators of NMDA-receptor activity. Recent data indicate that disturbances of glutamatergic transmission (especially via NMDA-receptor) are involved in pathogenesis of mood disorders. Magnesium deficiency, the same as disturbances in turn over of copper, are related to a variety of psychological symptoms especially depression. There are many reports indicating significant changes in blood levels of magnesium or copper during a depressive episode. Moreover magnesium exhibits antidepressant-like and anxiolytic-like effects in animal models of depression, in rodents. This article reviews the alterations in central and peripheral magnesium and copper homeostasis in relation to pathophysiology and treatment of depression.

Rôle du cuivre et du magnésium dans la pathogénie et le traitement de troubles affectifs

Le magnésium et le cuivre sont d'importants modulateurs de l'activité du récepteur NMDA. Des données récentes indiquent que des perturbations de la transmission glutamatergique (particulièrement via *le récepteur NMDA) sont impliquées dans la pathogénie des troubles de l'humeur. La déficience en magnésium, comme dans le renouvellement du cuivre, sont liées à plusieurs symptômes psychologiques et particulièrement la dépression. De nombreux rapports indiquent des changements significatifs des niveaux sanguins de magnésium ou de cuivre pendant un épisode dépressif. D'ailleurs, le magnésium montre des effets antidépresseurs et anxiolytiques dans le modèle animal de la dépression… Cet article passe en revue les altérations de l'homeostase du magnésium et du cuivre périphériques en relation avec la pathophysiologie et le traitement de la dépression.*

Ann Emerg Med. 1993 Jun;22(6):1028-34. ELSEVIER FULL-TEXT ARTICLE Links

Antagonists of excitatory amino acids and endogenous opioid peptides in the treatment of experimental central nervous system injury.

- Gentile NT,
- McIntosh TK.

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Trauma to the central nervous system can lead to primary injuries occurring at the time of impact as well as secondary or delayed injury processes that can result from cellular hypoxia, oligemia/ischemia, edema and swelling, and intracranial hypertension that are manifested over a period of hours to weeks after the initial event. Although the mechanisms underlying delayed tissue injury are poorly understood, they appear to be associated with endogenous neurochemical changes resulting from traumatic nervous system injury. These neurochemical changes may include excessive neurotransmitter release, deregulation of ion homeostasis, and the synthesis, release, or activation of various "autodestructive" neurochemical factors. Experimental studies over the past decade indicate that these alterations mediate important components of the neurochemical cascade leading to central nervous system injury. Furthermore, pharmacologic manipulations of these neurochemical changes have been reported to attenuate secondary central nervous system damage, ameliorate neuronal death, and promote functional recovery after central nervous system injury. This article focuses on the role of excitatory amino acid neurotransmitters, endogenous opioid peptides, and magnesium in the pathophysiology of central nervous system injury and on the therapeutic manipulation of these systems to improve functional outcome after central nervous system injury.

Les antagonistes des acides amines d'excitation et des peptides opioïdes endogènes dans le traitement d'une lésion expérimentale du SNC

Cet article est centré sur le rôle des aminoacides neurotransmetteurs excitateurs, des peptides opioïdes endogènes, et du magnésium dans la pathophysiologie d'une lésion du SNC et sur la manipulation thérapeutique de ces systèmes pour améliorer le résultat fonctionnel après la lésion du SNC.

Magnes Trace Elem. 1991-1992;10(2-4):263-8. Links

Magnesium deficiency in alcohol addiction and withdrawal.

- **Shane SR**,
- **Flink EB**.

Department of Medicine, University of Nevada School of Medicine, Reno.

The earliest description of clinical magnesium deficiency was reported in 1934. In 1954, Flink reported alcoholism as a cause of magnesium deficiency. This has been confirmed by low serum and tissue levels, balance studies, low exchangeable 28Mg and parenteral Mg retention tests. Alcohol causes urinary Mg wastage, but other mechanisms related to alcoholism contribute to the magnesium deficiency including malnutrition, gastrointestinal losses, phosphate deficiency, acidosis and/or alkalosis, vitamin D deficiency and free fatty acidemia associated with alcohol withdrawal. Mg replacement therapy is recommended to prevent some of the serious sequelae of magnesium deficiency.

Déficience en magnésium dans l'addiction à l'alcool et le sevrage

La première description de la déficience clinique en magnésium a été rapportée en 1934. En 1954, Flink présente l'alcoolisme comme une cause de déficience magnésienne. Cela a été confirmé (…). Une thérapie de remplacement en magnésium est recommandée pour prévenir certaines des graves séquelles dues à la déficience en magnésium.

Ter Arkh. 2004;76(11):97-9. Links

[Hypomagnesemia in patients with chronic alcoholism in the course of alcohol withdrawal syndrome]

[Article in Russian]

- **Stasiukinene VP**,
- **Pilvinis VK**,
- **Reingardene DI**.

AIM: To ascertain hypomagnesemia (HM) rate in patients with chronic alcoholism (CA) with alcohol withdrawal syndrome (AWS); correlation between AWS severity and HM rate. MATERIAL AND METHODS: Mg in plasm was measured at photometry in 129 CA patients treated in Kaunas Mental Hospital. RESULTS: Plasma Mg in CA patients with AWS was reduced (< 0.749 mmol/l), normal (0.750-1.250 mmol/l) or high (> 1.251 mmol/l) in 28.7, 65.1 and 6.2% patients, respectively. HM was diagnosed in 42.3% with a severe, 19.1% with a moderate and 20.0% with weak AWS. CONCLUSION: HM in AWS was registered in 28.7% patients. It occurred significantly more frequently ($p < 0.05$) in patients with a severe AWS. Pathogenetic mechanisms of HM in AWS are described.

L'hypomagnésie chez les patients alcooliques chroniques au cours du syndrome de sevrage alcoolique

L'hypomagnésémie dans le syndrome de sevrage a été enregistrée sur 28,7 % des patients. Elle se produit significativement plus fréquemment chez les patients avec un syndrome de sevrage sévère. Les mécanismes pathogéniques de l'hypomagnésémie dans le syndrome de sevrage ont été décrits.

Medicina (Kaunas). 2002;38(9):892-5. MEDICINA Free full text at MEDICINA.KMU.LT Links

[Blood plasma potassium, sodium and magnesium levels in chronic alcoholism during alcohol withdrawal]

[Article in Lithuanian]

- **Stasiukyniene V**.

Kauno medicinos universiteto Intensyviosios terapijos klinika, Mickeviciaus 9, 3000 Kaunas.

Blood plasma potassium, sodium and magnesium levels were studied in 114 chronic alcoholic patients (pts) during alcohol withdrawal. They were abnormal in 88.6% cases. Hypokalemia was observed in 28.9%, hyperkalemia--in 4.4%, hypomagnesemia in 29.8%, hypermagnesemia in 5.4%, hyponatremia in 72.8%, hypernatremia in 3.5% pts. In 23.7% cases disorders of two electrolytes and in 14% cases disorders of all three electrolytes for the same patient were established. Our data shows, that during alcohol withdrawal hyponatremia, hypomagnesemia and hypokalemia are not uncommon.

Va Med Q. 1997 Summer;124(3):184-7, 189. Links

Alcohol withdrawal.

- **Murray TD**,
- **Berger A**.

Turning Point Hospital for Chemical Dependency, Moultrie GA 31776-2471, USA.

There are three concurrent processes involved in the withdrawal from alcohol in an alcohol-dependent person. The first process is the hippocampal calcium channel mechanism diagnosed by the coarse tremor leading, sometimes precipitously, to convulsions. The second process is commonly referred to as alcoholic hallucinosis, and involves the psychoactive biogenic amine, harmine. The third process involves the locus coeruleus and presents as irritability, a fine tremor, autonomic storm, and diaphoresis. Magnesium and phenobarbital are usually sufficient to treat the syndrome of alcohol withdrawal, although neuroleptics may be required.

Alcohol Alcohol. 2004 Nov-Dec;39(6):486-92. Epub 2004 Oct 5.

Sevrage d'alcool

(…) Le magnésium et le phénobarbital sont habituellement suffisants pour traiter le syndrome de sevrage, quoique des neuroleptiques puissant être nécessaires.

Int J Addict. 1985 Apr;20(4):643-50. Links

Clinical experience with 781 cases of alcoholism evaluated and treated on an inpatient basis by various methods.

- **Daus AT**,
- **Freeman WM**,
- **Wilson J**,
- **Aponte C**.

A retrospective study of 781 alcoholics detoxified at two treatment centers suggested that magnesium sulfate was significant in preventing seizures and that benzodiazepines were essential in minimizing other complications. Future investigations should determine the most effective mineral dosage levels for alcohol detoxification.

Expérience clinique sur 781 cas d'alcooliques évalués et traités par différentes méthodes

Une étude rétrospective sur 781 alcooliques désintoxiqués dans deux centres de traitement suggèrent que le sulfate de magnésium est significatif dans la prévention des crises épileptiques et que les BZD sont essentielles pour minimiser les autres complications. De futures recherches devront déterminer les niveaux de dosage minéral les plus efficaces pour la désintoxication alcoolique.

Crit Care Resusc. 1999 Jun;1(2):162-72.

Intravenous magnesium.

- **Connolly E**,
- **Worthley LI**.

Department of Critical Care Medicine, Flinders Medical Centre, Adelaide, SA Australia.

OBJECTIVE: To review the function and use of intravenous magnesium in magnesium depleted and non-magnesium depleted patients. DATA SOURCES: A review of studies reported from 1966 to 1998 and identified through a MEDLINE search of the English-language literature on the use of intravenous magnesium. SUMMARY OF REVIEW: Magnesium is a metalo-coenzyme that participates in numerous enzymatic reactions including all reactions that involve the formation and utilization of ATP. The cardiovascular, neurological and metabolic disorders caused by magnesium deficiency are associated with an increase in morbidity and mortality and can be rapidly corrected by magnesium therapy. There is also evidence that intravenous magnesium alters ion channels, NMDA receptors, and calcium metabolism, causing effects that are beneficial in a range of cardiovascular, respiratory and metabolic disorders, in the absence of magnesium deficiency. In these disorders intravenous magnesium sulphate is usually administered as an initial bolus varying between 8 - 16 mmol over 5 min, followed by an infusion of 2 - 4 mmol/h, to keep the plasma magnesium between 1.5 - 3 mmol/L. CONCLUSIONS: Magnesium is required in patients who are magnesium depleted and is also of benefit in non-magnesium depleted

patients with pre-eclampsia. It may also be of benefit in non-magnesium depleted patients with acute coronary syndromes, arrhythmias, acute asthma, stroke, seizures and spinal cord injury.

Le magnésium intraveineux

(…) Sources de données: une revue des études rapportées de 1966 à 1998 et identifiées par une recherche MEDLINE de la littérature en anglais sur l'usage du magnésium intraveineux. (…) Conclusions : Le magnésium est nécessaire pour les patients dont le magnésium est déficitaire et il bénéficie aussi aux patient non-déficitaires souffrant de pré-éclampsie. Il peut aussi apporter un bénéfice aux patients non-déficitaires présentant des syndrome coronariens aigus, des arythmies, asthme aigu, AVC, crise d'épilepsie et des lésions de la moelle.

Anaesthesiol Reanim. 2003;28(1):13-20. Links

[Can alcoholic withdrawal delirium be prevented?]

[Article in German]

- **Hensel M**,
- **Kox WJ**.

Klinik fur Anasthesiologie und operative Intensivmedizin der Charite, Humboldt-Universitat zu Berlin.

In alcohol-dependent in-patients, an adequate drug prophylaxis should be made in order to lower the degree of a developing alcohol withdrawal syndrome (AWS) or to prevent a life-threatening delirium tremens. Pre-condition of successful therapy is a precise diagnosis. In patients, the beginning of whose abstinence is known, carefully-targeted pharmacological interventions can prevent severe imbalances of neurotransmitters. Typical time courses of destabilisation of neural balances should be considered. Since there is no single drug which is able to influence various transmitter systems, normally the use of drug combinations is necessary. In ENT-patients, traumatologic patients and patients from the department of maxillo-facial surgery, screening methods based on a simply-structured questionnaire relating to information from the patient and his surroundings and selected laboratory parameters should be used. High-risk patients who could get an AWS or delirium tremens should be treated prophylactically during their oral premedication period. Important drugs for successful prophylaxis of an AWS are benzodiazepines, clonidin, magnesium and vitamin B 1. A close-meshed control of the glucose metabolism, electrolyte and acid-base balance should be performed. Neuroleptica can be used if there is any indication for their adjuvant use. In severe cases that require deep sedation or hypnosis, propofol or gamma-hydroxy-butyric acid should be used. Perioperative infusion of alcohol as a prophylactic agent against delirium tremens is regarded as an obsolete therapeutic measure for ethical reasons and because equally good or better results can be achieved by carefully-targeted drug therapy. Due to its easy use, however, the application of alcohol has not yet completely disappeared from the therapeutic spectrum.

Le delirium lors du sevrage alcool peut-il être prévenu ?

(…) Les médicaments importants pour une prophylaxie efficace d'un syndrome de sevrage sont les BZD, la clonidine, le magnésium et la vitamine B1. (…)

J Neurochem. 1992 Aug;59(2):467-72. Links

Differential effects of Mg2+ and other divalent cations on the binding of tritiated opioid ligands.

- Rodriguez FD,
- Bardaji E,
- Traynor JR.

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The effects of MgCl2 on the binding of tritiated ligands to opioid binding sites in homogenates of guinea-pig brain in HEPES buffer have been studied. The binding of tritiated mu-, delta-, and kappa-opioid agonists was promoted in a concentration-dependent manner over a range of MgCl2 concentrations from 0.1 mM to 10 mM, as was binding of the nonselective antagonists [3H]diprenorphine and [3H]naloxone. At concentrations of MgCl2 above 10 mM reversal of this effect was observed. The effects of MgCl2 on binding parameters differed at each site. The promoting effects of MgCl2 were mimicked by MnCl2, CaCl2, and MgSO4, but CoCl2 and ZnCl2 were inhibitory. Following treatment of guinea-pig brain synaptosomes at pH 11.5 to eliminate G proteins, the binding of the mu-opioid agonist [3H][D-Ala2, MePhe4, Gly-ol5]enkephalin and [3H]naloxone was much reduced but binding of [3H]diprenorphine was unaffected. Under these conditions MgCl2 still promoted binding of [3H]diprenorphine. The results suggest that Mg2+ ions promote binding by an action at the opioid receptor, even in the absence of G protein, and that opioid antagonists may differ in their recognition of opioid receptor binding sites.

Différents effets du Mg2+ et d'autres cations divalents sur la liaison des ligands opioïdes connus.

(…) Ces résultats suggèrent que les ions Mg2+ favorisent la liaison par une action sur le récepteur opioïde, même en absence de protéine G, et que les antagonistes opioïdes peuvent différer dans leur reconnaissance des sites de liaison du récepteur opioïde.

Effects of CB1 cannabinoid receptor blockade on ethanol preference after chronic alcohol administration combined with repeated re-exposures and withdrawals.

- Lallemand F,
- Soubrie P,
- De Witte P.

Laboratoire Biologie du Comportement, Universite Catholique de Louvain, 1 Croix du Sud, 1348 Louvain-la-Neuve, Belgium.

AIMS: The cannabinoid CB1 receptor antagonist, SR141716A, differentially affects the ethanol preference of chronically alcoholized rats when administered during cycles of ethanol exposure and withdrawal. In this study, ethanol preference was investigated in chronically alcoholized rats that underwent regular withdrawal periods during which the brain cannabinoid CB(1) receptor antagonist, SR141716A, was administered. METHODS: The cannabinoid receptor antagonist SR141716A, 3 or 10 mg/kg/day, was administered i.p. to Wistar rats at the conclusion of a 4-week period of chronic alcoholization, as they commenced a cycle of alcohol withdrawal for 10 days followed by a period of 10 days chronic ethanol exposure. In a second set of experiments, an additional cycle of ethanol withdrawal and re-exposure was given. Preference for ethanol versus water started at the end of the first or second chronic ethanol re-exposure for a period of at least 30 days. RESULTS: In rats pretreated with the higher dose of SR141716A, ethanol preference during free choice was significantly increased after two ethanol re-exposures. In contrast, pretreatment with the lower SR141716A dose induced no significant change in ethanol intake during the free choice followed by either one or two ethanol re-exposures. CONCLUSIONS: SR141716A, 10 mg/kg/day dose, induced a significant increase in ethanol preference which was dependent on both the number of ethanol withdrawals and chronic ethanol re-exposures, while 3 mg/kg/day had no significant effect on ethanol preference.

Altern Med Rev. 2006 Dec;11(4):294-9.

Peripheral neuropathy: pathogenic mechanisms and alternative therapies.

- Head KA.

Technical Advisor, Thorne Research, Inc.; Editor-In-Chief, Alternative Medicine Review. Correspondence address: Thorne Research, PO Box 25, Dover, ID 83825.

Peripheral neuropathy (PN), associated with diabetes, neurotoxic chemotherapy, human immunodeficiency virus (HIV)/antiretroviral drugs, alcoholism, nutrient deficiencies, heavy metal toxicity, and other etiologies, results in significant morbidity. Conventional pain medications primarily mask symptoms and have significant side effects and addiction profiles. However, a widening body of research indicates alternative medicine may offer significant benefit to this patient population. Alpha-lipoic acid, acetyl-L-carnitine, benfotiamine, methylcobalamin, and topical capsaicin are among the most well-researched alternative options for the treatment of PN. Other potential nutrient or botanical therapies include vitamin E, glutathione, folate, pyridoxine, biotin, myo-inositol, omega-3 and -6 fatty acids, L-arginine, L-glutamine, taurine, N-acetylcysteine, zinc, magnesium, chromium, and St. John's wort. In the realm of physical medicine, acupuncture, magnetic therapy, and yoga have been found to provide benefit. New cutting-edge conventional therapies, including dual-action peptides, may also hold promise.

Eksp Klin Farmakol. 2003 Sep-Oct;66(5):40-4. Links

[Study of pharmacological activity of complex magnesium-containing preparation based on mineral bishofit and pyridoxine hydrochloride in a rat model of chronic alcoholic intoxication]

[Article in Russian]

- Spasov AA,
- Petrov VI,
- Iezhitsa IN,
- Onishchenko NV,
- Churbakova NV,
- Parshev VV.

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Nervous disturbances accompanying alcoholic illness were studied in relation to the depletion of magnesium ion content in the organism. The possibility of correcting the development of psychic (behavioral) pathologies by treatment with a complex magnesium-containing preparation based on mineral bishofit and pyridoxine hydrochloride (below, Mg-containing preparation) was studied in rats upon three-month voluntary alcoholization. A decrease in the locomotor (number of crossed squares) and vertical (number of standings) activity as evaluated in the open-field test and an increase in the immobilization time in the forced swim test showed evidence of depressive state in animals after long-term ethanol administration. After treatment with the Mg-containing preparation (50 mg Mg/kg in 2.5 ml volume, p.o.), the immobilization time of alcohol-preferring rats decreased in comparison to that before treatment and showed no statistically significant differences from the value in the intact control group. A decrease in the immobilization time (the main sign of antidepressant action) allows the Mg-containing preparation to be considered as antidepressant. The level of magnesium in rat blood erythrocytes decreased upon three-month voluntary alcoholization by 40.95 +/- 2.41% relative to control ($p < 0.05$). After a 5-week treatment with Mg-containing preparation under conditions of free access to alcohol, the content of magnesium in the erythrocytes of alcohol-preferring rats restored on a normal level. Chronic alcoholism reduces the content of microelements and vitamins (in particular, B6), these changes being mutually related.