GB
„Thiamine-dependent processes and treatment strategies in neurodegeneration.“

DE
Thiamin-abhängige Prozesse und Behandlungsstrategien bei Neurodegeneration.

GR
Θειαμινο-εξαρτώμενες διαδικασίες και στρατηγικές θεραπείας στο νευροεκφυλισμό.

FR
Processus dépendant de la thiamine et stratégies de traitement dans la neurodégénérescence.

CZ
Procesy závislé na thiaminu a léčebné strategie při neurodegeneraci.

Antioxid Redox Signal. 2007 Oct;9(10):1605-19.

Thiamine-dependent processes and treatment strategies in neurodegeneration.

Gibson GE, Blass JP.

Source Department of Neurology and Neurosciences, Weill Medical College of Cornell University, Burke Medical Research Institute, White Plains, New York 10605, USA. ggibson@med.cornell.edu

Reductions in brain glucose metabolism and increased oxidative stress invariably occur in Alzheimer's disease (AD) and thiamine (vitamin B1) deficiency. Both conditions cause irreversible cognitive impairment; their behavioral consequences overlap but are not identical. Thiamine-dependent processes are critical in glucose metabolism, and recent studies implicate thiamine in oxidative stress, protein processing, peroxisomal function, and gene expression. The activities of thiamine-dependent enzymes are characteristically diminished in AD, and the reductions in autopsy AD brain correlate highly with the extent of dementia in the preagonal state. Abnormalities in thiamine-dependent processes can be plausibly linked to the pathology of AD. Seemingly paradoxical properties of thiamine-dependent processes may underlie their relation to the pathophysiology of AD: Reduction of thiamine-dependent processes increase oxidative stress. Thiamine can act as a free radical scavenger. Thiamine-dependent mitochondrial dehydrogenase complexes produce oxygen free radicals and are sensitive to oxidative stress. Genetic disorders of thiamine metabolism that lead to neurological disease can be treated with large doses of thiamine. Although thiamine itself has not shown dramatic benefits in AD patients, the available data is scanty. Adding thiamine or more absorbable forms of thiamine to tested treatments for the abnormality in glucose metabolism in AD may increase their efficacy.

PMID: 17685850

GB
„Interactions of oxidative stress with thiamine homeostasis promote neurodegeneration.“

DE
Die Interaktion von oxidativem Stress mit der Thiamin-Homöostase fördert die Neurodegeneration.

GR
Αλληλεπιδράσεις μεταξύ του οξειδωτικού στρες και της ομοιόστασης της θειαμίνης προάγουν το νευροεκφυλισμό.

FR
Les interactions du stress oxydatif avec l‘homéostasie de la thiamine promeuvent la neurodégénérescence.

CZ
Interakce oxidačního stresu s homeostázou thiaminu podporují neurodegeneraci.

Neurochem Int. 2002 May;40(6):493-504.

Interactions of oxidative stress with thiamine homeostasis promote neurodegeneration.

Gibson GE, Zhang H.

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Abstract

Thiamine-dependent processes are diminished in brains of patients with several neurodegenerative diseases. The decline in thiamine-dependent enzymes can be readily linked to the symptoms and pathology of the disorders. Why the reductions in thiamine linked processes occur is an important experimental and clinical question. Oxidative stress (i.e. abnormal metabolism of free radicals) accompanies neurodegeneration and causes abnormalities in thiamine-dependent processes. The vulnerability of thiamine homeostasis to oxidative stress may explain deficits in thiamine homeostasis in numerous neurological disorders. The interactions of thiamine with oxidative processes may be part of a spiral of events that lead to neurodegeneration, because reductions in thiamine and thiamine-dependent processes promote neurodegeneration and cause oxidative stress. The reversal of the effects of thiamine deficiency by antioxidants, and amelioration of other forms of oxidative stress by thiamine, suggest that thiamine may act as a site-directed antioxidant. The data indicate that the interactions of thiamine-dependent processes with oxidative stress are critical in neurodegenerative processes.

PMID: 11850106

GB
„Effect of B vitamins-fortified foods on primary school children in Beijing.“

DE
Die Wirkung von mit B-Vitaminen angereicherten Nahrungsmitteln auf Grundschulkinder in Peking.

GR
Αποτελέσματα από την κατανάλωση ενισχυμένων με βιταμίνες Β τροφών σε μαθητές πρωτοβάθμιας εκπαίδευσης στο Πεκίνο.

FR
Effets des aliments enrichis en vitamines B sur les enfants d‘école primaire à Pékin.

CZ
Účinek potravin obohacených vitamíny skupiny B na děti na základních školách v Pekingu.

Asia Pac J Public Health. 2006;18(2):21-5.

Effect of B vitamins-fortified foods on primary school children in Beijing.

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Abstract

The objective of this study is to investigate the effect of B vitamins-fortified foods on primary school children. A controlled trial was conducted in 101 normal primary school children aged 9-11 years. They were randomly assigned to supplemental control group (S-control, n=36), riboflavin supplementation group (+riboflavin 0.625 mg/day, n=32), and B vitamin compound supplementation group (+riboflavin 0.625 mg/day, +thiamin 0.512 mg/day, +nicotinic acid 0.365 mg/day, +folic acid 0.13 mg/day, n=33) based on school classes. Urinary riboflavin excretion and erythrocyte glutathione reductase activity coefficient (EGRAC) along with erythrocyte transketolase activity (ETKA) were used to evaluate B vitamin levels in the children. AYP index, an index reflecting the brain performance ability, was chosen to assess the children's study abilities. Health education was carried out to help children and their parents adopt scientific dietary concepts. The urinary riboflavin excretion was higher in two supplementation groups (435.24 +/- 153.3 microg/g creatinine, 374.6 +/- 144.6 microg/g creatinine) than in S-control group (235.1 +/- 86.2 microg/g creatinine). Average values of EGRAC were lower in two supplementation groups (0.90 +/- 0.11, 0.80 +/- 0.10) than in S-control group (1.08 +/- 0.25). At the same time, the percentage of thiamine pyrophosphate (TPP%) decreased from 63.69 +/- 28.04 to 42.16 +/- 16.31 in B vitamin compound supplementation group. Meanwhile, AYP index increased at the end of the supplementation in two supplementation groups**. B vitamins supplementation can significantly increase B vitamin level in children. Biochemical activities of riboflavin and thiamin can improve with the intake of fortified foods. The effect of B vitamin compound supplementation is better than that of single riboflavin supplementation** when the effect of riboflavin's biofunction is considered. **In**

addition, micronutrient supplementation appears to assist children's study abilities.

PMID: 16883966

GB
„Thiamine and oxidants interact to modify cellular calcium stores.“

DE
Die Interaktion von Thiamin und Oxidanzien führt zur Modifikation der zellulären Calciumspeicher.

GR
Η θειαμίνη και τα αντιοξειδωτικά αλληλεπιδρούν για την τροποποίηση των κυτταρικών αποθεμάτων ασβεστίου.

FR
La thiamine et les oxydants interagissent pour modifier les réserves cellulaires de calcium.

CZ
Thiamin a oxidanty se vzájemně ovlivňují za účelem modifikace buněčných usazenin vápníku.

Neurochem Res. 2010 Dec;35(12):2107-16. doi: 10.1007/s11064-010-0242-z. Epub 2010 Aug 24.

Thiamine and oxidants interact to modify cellular calcium stores.

Huang HM, Chen HL, Gibson GE.

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AbstractDiminished thiamine (vitamin B1) dependent processes and oxidative stress accompany Alzheimer's disease (AD). Thiamine deficiency in animals leads to oxidative stress. These observations suggest that thiamin may act as an antioxidant. The current experiments first tested directly whether thiamin could act as an antioxidant, and then examined the physiological relevance of the antioxidant properties on oxidant sensitive, calcium dependent processes that are altered in AD. The first group of experiments examined whether thiamin could diminish reactive oxygen species (ROS) or reactive nitrogen species (RNS) produced by two very divergent paradigms. Dose response curves determined the concentrations of t-butyl-hydroperoxide (t-BHP) (ROS production) or 3-morpholinosydnonimine ((SIN-1) (RNS production) to induce oxidative stress within cells. Concentrations of thiamine that reduced the RNS in cells did not diminish the ROS. The second group of experiments tested whether thiamine alters oxidant sensitive aspects of calcium regulation including endoplasmic reticulum (ER) calcium stores and capacitative calcium entry (CCE). Thiamin diminished ER calcium considerably, but did not alter CCE. Thiamine did not alter the actions of ROS on ER calcium or CCE. On the other hand, thiamine diminished the effect of RNS on CCE. These data are consistent with thiamine diminishing the actions of the RNS, but not ROS, on physiological targets. Thus, both experimental approaches suggest that thiamine selectively alters RNS. Additional experiments are required to determine whether diminished thiamine availability promotes oxidative stress in AD or whether the oxidative stress in AD brain diminishes thiamine availability to thiamine dependent processes.

PMID: 20734230

GB

„Thiamine deficiency induces oxidative stress and exacerbates the plaque pathology in Alzheimer‘s mouse model.“

DE

„Thiaminmangel induziert oxidativen Stress und verschlimmert die Plaquepathologie im Alzheimer-Mausmodell.“

GR

„Η έλλειψη θειαμίνης προκαλεί οξειδωτικό στρες και επιδεινώνει την παθολογία πλάκας στο μοντέλο Αλτσχάιμερ με ποντίκια.“

FR

Les carences en thiamine induisent un stress oxydatif et exacerbent la pathologie plaquettaire sur le modèle avec souris atteinte d‘Alzheimer.

CZ

Nedostatek thiaminu vyvolává oxidační stres a zhoršuje patologii plátu u myšího modelu Alzheimerovy choroby.

Neurobiol Aging. 2009 Oct;30(10):1587-600. doi: 10.1016/j.neurobiolaging.2007.12.013. Epub 2008 Apr 10.

Thiamine deficiency induces oxidative stress and exacerbates the plaque pathology in Alzheimer's mouse model.

Karuppagounder SS, Xu H, Shi Q, Chen LH, Pedrini S, Pechman D, Baker H, Beal MF, Gandy SE, Gibson GE.

Source Department of Neurology and Neurosciences, Weill Medical College of Cornell University, Burke Medical Research Institute, 785 Mamaroneck Avenue, White Plains, NY 10605, USA.

Mitochondrial dysfunction, oxidative stress and reductions in thiamine-dependent enzymes have been implicated in multiple neurological disorders including Alzheimer's disease (AD). Experimental thiamine deficiency (TD) is an established model for reducing the activities of thiamine-dependent enzymes in brain. TD diminishes thiamine-dependent enzymes throughout the brain, but produces a time-dependent selective neuronal loss, glial activation, inflammation, abnormalities in oxidative metabolism and clusters of degenerating neurites in only specific thalamic regions. The present studies tested how TD alters brain pathology in Tg19959 transgenic mice over expressing a double mutant form of the amyloid precursor protein (APP). TD exacerbated amyloid plaque pathology in transgenic mice and enlarged the area occupied by plaques in cortex, hippocampus and thalamus by 50%, 200% and 200%, respectively. TD increased Abeta(1-42) levels by about three fold, beta-CTF (C99) levels by 33% and beta-secretase (BACE1) protein levels by 43%. TD-induced inflammation in areas of plaque formation. Thus, the induction of mild impairment of oxidative metabolism, oxidative stress and inflammation induced by TD alters metabolism of APP and/or Abeta and promotes accumulation of plaques independent of neuron loss or neuritic clusters.

PMID: 18406011

GB
„The Impact of Oxidative Stress in Thiamine Deficiency: A Multifactorial Targeting Issue.“

DE
Der Einfluss von oxidativem Stress bei Thiaminmangel: Ein multifaktorielles Targetingproblem.

GR
Η Επίπτωση του Οξειδωτικού Στρες στην Έλλειψη Θειαμίνης: ένας πολυπαραγοντικός στόχος.

FR
L‘impact du stress oxydatif dans la carence en thiamine : une problème de ciblage multifactoriel.

CZ
„Vliv oxidačního stresu při nedostatek thiaminu: multifaktorově cílený problém.„

Neurochem Int. 2013 Jan 17. pii: S0197-0186(13)00012-0. doi: 10.1016/j.neuint.2013.01.009. [Epub ahead of print]

The Impact of Oxidative Stress in Thiamine Deficiency: A Multifactorial Targeting Issue.

Hazell AS, Faim S, Wertheimer G, Silva VR, Marques CS.

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Abstract

Thiamine (vitamin B1) deficiency, the underlying cause of Wernicke-Korsakoff syndrome, is associated with the development of focal neuronal loss in vulnerable areas of the brain. Although the actual mechanism(s) that lead to the selective histological lesions characteristic of this disorder remain unresolved, oxidative stress has been shown to play a major role in its pathophysiology. **In this review, the multifactorial influence of oxidative stress on a variety of processes known to take part in the development of structural lesions in TD including excitotoxicity, neuroinflammation, blood-brain barrier integrity, mitochondrial integrity, apoptosis, nucleic acid function, and neural stem cells will be discussed, and therapeutic strategies undertaken for treating neurodegeneration examined which may have an impact on the future treatment of this important vitamin deficiency.**

PMID: 23333339

GB

„Update of cell damage mechanisms in thiamine deficiency: focus on oxidative stress, excitotoxicity and inflammation.“

DE

Update zu Zellschädigungsmechanismen bei Thiaminmangel: Fokus auf oxidativem Stress, Excitotoxizität und Inflammation.

GR

„Ενημέρωση των μηχανισμών φθοράς κυττάρων στην έλλειψη θειαμίνης: έμφαση στο οξειδωτικό στρες, τη διεγερσιτοξικότητα και τη φλεγμονή.“

FR

Actualisation des mécanismes de lésionnement cellulaire dans la carence en thiamine : focus sur le stress oxydatif, l‘excitotoxicité et l‘inflammation.

CZ

Obnovení mechanizmů poškození buněk při nedostatku thiaminu: zaměření na oxidační stres, excitotoxicitu a inflamaci.

Alcohol Alcohol. 2009 Mar-Apr;44(2):141-7. doi: 10.1093/alcalc/agn120. Epub 2009 Jan 16.

Update of cell damage mechanisms in thiamine deficiency: focus on oxidative stress, excitotoxicity and inflammation.

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Abstract

Thiamine deficiency (TD) is a well-established model of Wernicke's encephalopathy. Although the neurologic dysfunction and brain damage resulting from the biochemical consequences of TD is well characterized, the mechanism(s) that lead to the selective histological lesions characteristic of this disorder remain a mystery. Over the course of many years, various structural and functional changes have been identified that could lead to cell death in this disorder. However, despite a concerted effort to explain the consequences of TD in terms of these changes, our understanding of the pathophysiology of this disorder remains unclear. This review will focus on three of these processes, i.e. oxidative stress, glutamate-mediated excitotoxicity and inflammation and their role in selective vulnerability in TD. Since TD inhibits oxidative metabolism, a feature of many neurodegenerative disease states, it represents a model system with which to explore pathological mechanisms inherent in such maladies, with the potential to yield new insights into their possible treatment and prevention.

PMID: 19151161

GB
Molecular mechanisms of thiamine utilization.

DE
Molekulare Mechanismen der Thiaminverwendung.

GR
Μοριακοί μηχανισμοί της χρήσης θειαμίνης.

FR
Mécanismes moléculaires d'utilisation de la thiamine.

CZ
Molekulární mechanizmy využití thiaminu.

Curr Mol Med. 2001 May;1(2):197-207.

Molecular mechanisms of thiamine utilization.

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Abstract

Thiamine is required for all tissues and is found in high concentrations in skeletal muscle, heart, liver, kidneys and brain. A state of severe depletion is seen in patients on a strict thiamine-deficient diet in 18 days, but the most common cause of thiamine deficiency in affluent countries is alcoholism. Thiamine diphosphate is the active form of thiamine, and it serves as a cofactor for several enzymes involved primarily in carbohydrate catabolism. The enzymes are important in the biosynthesis of a number of cell constituents, including neurotransmitters, and for the production of reducing equivalents used in oxidant stress defenses and in biosyntheses and for synthesis of pentoses used as nucleic acid precursors. Because of the latter fact, thiamine utilization is increased in tumor cells. Thiamine uptake by the small intestines and by cells within various organs is mediated by a saturable, high affinity transport system. Alcohol affects thiamine uptake and other aspects of thiamine utilization, and these effects may contribute to the prevalence of thiamine deficiency in alcoholics. The major manifestations of thiamine deficiency in humans involve the cardiovascular (wet beriberi) and nervous (dry beriberi, or neuropathy and/or Wernicke-Korsakoff syndrome) systems. A number of inborn errors of metabolism have been described in which clinical improvements can be documented following administration of pharmacological doses of thiamine, such as thiamine-responsive megaloblastic anemia. Substantial efforts are being made to understand the genetic and biochemical determinants of inter-individual differences in susceptibility to development of thiamine deficiency-related disorders and of the differential vulnerabilities of tissues and cell types to thiamine deficiency.

PMID: 11899071

GB
„Thiamine deficiency-related brain dysfunction in chronic liver failure.“

DE
Thiaminmangel-bedingte Hirndysfunktion bei chronischem Leberversagen.

GR
Εγκεφαλική δυσλειτουργία που σχετίζεται με έλλειψη θειαμίνης στη χρόνια ηπατική ανεπάρκεια.

FR
Dysfonctionnement du cerveau lié à une carence en thiamine, dans la défaillance hépatique chronique.

CZ
Mozková dysfunkce v důsledku nedostatku thiaminu při chronickém selhání jater.

Metab Brain Dis. 2009 Mar;24(1):189-96. doi: 10.1007/s11011-008-9129-y. Epub 2008 Dec 6.

Thiamine deficiency-related brain dysfunction in chronic liver failure.

Butterworth RF.

Source Neuroscience Research Unit, Saint-Luc Hospital (CHUM), University of Montreal, 1058, Saint-Denis Street, Montreal, QC H2X 3J4, Canada. roger.butterworth@umontreal.ca

Abstract

End-stage chronic liver failure results in thiamine deficiency caused principally by depletion of liver thiamine stores. Chronic liver failure also leads to increased brain ammonia concentrations. Both ammonia and thiamine deficiency result in decreased activity of alpha-ketoglutarate dehydrogenase, a rate-limiting tricarboxylic acid cycle enzyme. Loss of enzyme activity results in a mitochondrial oxidative deficit in brain and consequent increases in brain lactate, oxidative/nitrosative stress, cellular energy impairment and release of proinflammatory cytokines, all of which have been described in brain in end-stage chronic liver failure. Synergistic effects of ammonia exposure and thiamine deficiency could explain the diencephalic and cerebellar symptomatology described in patients with "hepatic encephalopathy". Unsuspected brain lesions due to thiamine deficiency could explain the incomplete resolution of neuropsychiatric symptoms following the use of ammonia-lowering agents or liver transplantation in patients with end-stage chronic liver failure. These findings underscore the need for prompt, effective thiamine supplementation in all patients with chronic liver failure.

PMID: 19067139