

Table 3. Studies reporting effects on the Brain from Fluoride		
Study	Dose	Effect
<p>Biometals. 2005 Jun; 18(3): 207-12.</p> <p>Exposure to high fluoride concentration in drinking water will affect spermatogenesis and steroidogenesis in male albino rats.</p> <p>Pushpalatha T, Srinivas M, Sreenivasula Reddy P.</p> <p>Department of Biotechnology, Sri Venkateswara University, Tirupati - 517 502, India. □</p>	<p>RAT – adult Wistar males</p> <p>NaF in drinking water</p> <p>4.5 and 9.0 ppm for 75 days</p> <p>Abstract</p> <p>FULL STUDY available at Science Direct</p>	<p>Significant decrease in brain index.</p>
<p>Wei Sheng Yan Jiu. 2004 Mar;33(2):158-61.</p> <p>[Influence of combined iodine and fluoride on phospholipid and fatty acid composition in brain cells of rats]</p> <p>Shen X, Zhang Z, XU X.</p> <p>College of Life and Environment Science, Zhejiang Normal University, Jinhua 321004, China.</p>	<p>RAT</p> <p>Five groups of rats were provided with deionized drinking water containing 0 and 150 mg/L NaF, and containing both 150 mg/L NaF and 0.003, 0.03 or 3 mg/L KI respectively for 5 months</p> <p>Abstract</p>	<p>CONCLUSION: Fluorosis had obvious influence on phospholipid and fatty acid composition in brain cells of rats, and its mechanism might be associated with action of lipid peroxidation, and 0.03 mg/L KI is the optimal concentration for the antagonistic action with this influence from fluorosis.</p>
<p>Fluoride 2003 Vol. 36 No. 4 263-266</p> <p>FLUORIDE CONTENT IN SOFT TISSUES AND URINE OF RATS EXPOSED TO SODIUM FLUORIDE IN DRINKING WATER</p> <p>I Inkielewicz, J Krechniak</p> <p>Department of Toxicology, Medical University of Gdańsk, Poland.</p>	<p>RAT</p> <p>Eight-week-old male Wistar rats</p> <p>NaF in drinking water of 5 and 25 mg F- /L for 12 weeks</p> <p>Controls received tap water containing 0.3 mg F - /L</p> <p>FULL STUDY</p>	<p>The fluoride content in liver, kidney, brain, and testis increased in a dose-dependent and a time-dependent manner. In animals receiving the higher dose of NaF the increase after 12 weeks of exposure was about two-fold in serum, seven-fold in liver and kidney, NINE-FOLD in BRAIN, and TWELVE FOLD IN TESTIS.</p>
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<p>Zhonghua Lao Dong Wei Sheng Zhi Ye Bing Za Zhi. 2003 Apr; 21(2):102-4.</p> <p>[Studies on fluoride concentration and cholinesterase activity in rat hippocampus]</p> <p>Zhai JX, Guo ZY, Hu CL, Wang QN, Zhu QX.</p> <p>School of Public Health, Anhui Medical University, Hefei 230032, China. □</p>	<p>RAT</p> <p>high dosage group: (13.03 +/- 1.79) micro g/g</p> <p>low dosage group: (9.83 +/- 0.92) micro g/g</p> <p>Abstract</p>	<p>Fluoride concentration in rat hippocampus was significantly correlated with the dosage of fluoride, and there were significant differences among high dosage group, low dosage group, and control.</p> <p>CONCLUSION: Fluoride may go through the blood-brain barrier and accumulate in rat hippocampus, and inhibit the activity of cholinesterase.</p>
<p>Fluoride 2003. 36: 95-105.</p> <p>Histopathological investigation of fluoride-induced neurotoxicity in rabbits.</p> <p>Shashi A.</p>	<p>RABBIT</p> <p>NaF 0, 5, 10, 20, and 50 mg</p> <p>15 weeks</p> <p>FULL STUDY</p>	<p>Neuropathological changes occurred with loss of the molecular layer and glial cell layer in the brain tissues of rabbits exposed to the three higher fluoride doses. The Purkinje neurones exhibited chromatolysis and acquired a "ballooned" appearance. Nissl substance showed various degrees of decrease and even complete loss. Fragmented particles were retained in the perinuclear zone. The perikaryon showed vacuolization, and spheroid bodies were present in the neoplasm.</p>
<p>Toxicology. 2003 Feb 1;183(1-3):235-42.</p> <p>Selective decreases of nicotinic acetylcholine receptors in PC12 cells exposed to fluoride.</p> <p>Chen J, Shan KR, Long YG, Wang YN, Nordberg A, Guan ZZ.</p> <p>Department of Pathology, Guiyang Medical College, Guiyang 550004, Guizhou, PR China.</p>	<p>PC12 cells, a rat pheochromocytoma cell line grown in RPMI 1640 medium</p> <p>Incubated with different doses of NaF for 48 h at 37° C.</p> <p>Abstract. FULL STUDY at Science Direct.</p>	<p>In an attempt to elucidate the mechanism by which excessive fluoride damages the central nervous system, the effects of exposure of PC12 cells to different concentrations of fluoride for 48 h on nicotinic acetylcholine receptors (nAChRs) were characterized.</p> <p>findings suggest that selective decreases in the number of nAChRs may play an important role in the mechanism(s) by which fluoride causes dysfunction of the central nervous system. Note: nAChRs play major roles in cognitive processes such as learning and memory.</p>
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<p>Indian J Exp Biol. 2002 May;40(5):546-54.</p> <p>Neurotoxicity of fluoride: neurodegeneration in hippocampus of female mice.</p> <p>Bhatnagar M, Rao P, Sushma J, Bhatnagar R.</p> <p>Dept. of Zoology, M.L.S. University, Udaipur, India.</p>	<p>MOUSE (Female)</p> <p>Abstract</p>	<p>Ultrastructural studies revealed neurodegenerative characteristics like involution of cell membranes, swelling of mitochondria, clumping of chromatin material etc, can be observed in cell bodies of CA3, CA4 and dentate gyrus (Dg).</p> <p>Fluoride intoxicated animals also performed poorly in motor co-ordination tests and maze tests</p>
<p>Zhonghua Yu Fang Yi Xue Za Zhi. 2002 Jul;36(4):222-4.</p> <p>[Studies on DNA damage and apoptosis in rat brain induced by fluoride]</p> <p>Chen J, Chen X, Yang K, Xia T, Xie H.</p> <p>Dept. of Environmental Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China.</p>	<p>RAT</p> <p>NaF</p> <p>SD rats were divided into two groups, i.e. control group and fluoride treated group, which were injected intraperitoneally with distilled water and sodium fluoride (20 mg.kg(-1).d(-1)) respectively. 5 mmol/L NaF were used in in vitro study.</p> <p>Abstract</p>	<p>The DNA damage in pallium neurons in rats of the fluoride group was much more serious compared with those of the control group</p> <p>TUNEL positive cells were found in pallium, hippocampus and cerebellar granule cells in rats of fluoride group, whereas those in the control group were rare</p>
<p>Fluoride 2002; 35(3):153-160.</p> <p>Brain lipid peroxidation and antioxidant systems of young rats in chronic fluoride intoxication.</p> <p>Shivarajashankara YM*, Shivashankara AR, Bhat PG, Rao SH</p> <p>* Dept. of Biochemistry, MR Medical College, Gulbarga-585105, Karnataka, India.</p>	<p>RAT</p> <p>NaF</p> <p>FULL STUDY</p>	<p>results suggest that fluoride enhances oxidative stress in the brain, thereby disturbing the antioxidant defense of rats Increased oxidative stress could be one of the mediating factors in the pathogenesis of fluoride toxicity in the brain.</p>
<p>Fluoride 2002; 35(1):12-21</p> <p>Histological changes in the brain of young fluoride-intoxicated rats</p> <p>YM Shivarajashankara*, AR Shivashankara, P Gopalakrishna Bhat, S Muddanna Rao, S Hanumanth Rao</p>	<p>RAT</p> <p>100 ppm F</p> <p>FULL STUDY</p>	<p>significant neurodegenerative changes in the hippocampus, amygdala, motor cortex, and cerebellum. Changes included decrease in size and number of neurons in all the regions, decrease in the number of Purkinje cells in the cerebellum, and signs of chromatolysis and gliosis in the motor cortex.</p>
<p>Continued ...</p>		

<p>Neurotoxicol Teratol 2002 Nov-Dec;24(6):751-7</p> <p>Chronic fluoride toxicity decreases the number of nicotinic acetylcholine receptors in rat brain.</p> <p>Long YG, Wang YN, Chen J, Jiang SF, Nordberg A, Guan ZZ.</p> <p>Dept. of Pathology, Guiyang Medical College, 550004, Guizhou, Guiyang, PR China</p>	<p>RAT</p> <p>30 or 100 ppm F in their drinking water for 7 months</p> <p>Abstract</p> <p>FULL STUDY at Science Direct</p>	<p>There was a significant reduction in the number of [3H]epibatidine binding sites in the brain of rats exposed 100 ppm of fluoride... the number of [125I]alpha-BTX binding sites was significantly decreased in the brains of rats exposed to both levels of fluoride. Western blotting revealed that the level of the nAChR alpha4 subunit protein in the brains of rats was significantly lowered by exposure to 100 ppm, but not 30 ppm fluoride; whereas the expression of the alpha7 subunit protein was significantly decreased by both levels of exposure.</p> <p>Since nAChRs play major roles in cognitive processes such as learning and memory, the decrease in the number of nAChRs caused by fluoride toxicity may be an important factor in the mechanism of brain dysfunction in the disorder.</p>
<p>Wei Sheng Yan Jiu 2001 May;30(3):144-6</p> <p>[Effects of selenium on the damage of learning-memory ability of mice induced by fluoride]</p> <p>Zhang Z, Shen X, Xu X.</p> <p>College of Life and Environmental Science, Zhejiang Normal University, Jinhua 321004, China.</p>	<p>MOUSE (male)</p> <p>NaF added with or without sodium selenite in deionized water was administered to male mice for 8 weeks.</p> <p>Abstract</p>	<p>The influences of fluoride on learning-memory behavior were tested on Y-maze, and the ultrastructure of Gray I synaptic interface in the CA3 area hippocampus was quantitatively analyzed by electron microscopy and computer image processing appliance.</p> <p>The main results showed that the learning capability of mice drinking higher concentration of fluoride presented remarkable deterioration.</p> <p>The results suggested that selenium might antagonize the neurotoxicity of fluoride on behavior and morphology.</p>
<p>Continued ...</p>		

<p>Fluoride 2001; 34(3):165-173</p> <p>Effect of fluoride on thyroid function and cerebellar development in mice</p> <p>Mahmoud Trabelsi, Fadhel Guermazi, Najiba Zeghal*</p> <p>* Animal Physiology Laboratory, Dept. of Biology, Faculty des Sciences de Sfax-Route de la Soukra-Km 3.5, 3038 Sfax BP802, Tunisia.</p>	<p>MOUSE</p> <p>NaF in drinking water (0.5 g/L) to pregnant and lactating mice, from the 15th day of pregnancy to the 14th day after delivery.</p> <p>FULL STUDY</p>	<p>Compared to the control group, reductions in the cerebellar and cerebral protein concentrations by 27% and 17%, respectively.</p> <p>Consistent histological changes were present in the cerebellum of the treated mice with the external granular layer being markedly reduced or absent, the Purkinje cell bodies being poorly differentiated and arranged in a single layer at the surface of the internal granular layer, and with more apoptotic Purkinje cells being present.</p>
<p>Fluoride 2001; 34(2):108-113</p> <p>Effect of fluoride intoxication on lipid peroxidation and antioxidant systems in rats</p> <p>YM Shivarajashankara, AR Shivashankara, P Gopalakrishna Bhat, S Hanumanth Rao</p>	<p>RAT</p> <p>12 one-month-old albino rats were administered 100-ppm fluoride (as NaF) in their drinking water for 4 months.</p> <p>FULL STUDY</p>	<p>In the brain and liver, MDA and GSH levels increased, as did the activities of GSH-Px and glutathione S-transferase (GST). The level of ascorbic acid increased in the brain, but it decreased in the liver. These results suggest that fluoride enhances lipid peroxidation in the red blood cells, brain and liver of rats and causes increased or decreased enzyme activity associated with free radical metabolism.</p>
<p>Wei Sheng Yan Jiu 2000 Jul;29(4):216-7</p> <p>[Effects of selenium and zinc on the DNA damage caused by fluoride in pallium neural cells of rats]</p> <p>Chen J, Chen X, Yang K.</p> <p>Dept. of Environmental Health, Tongji Medical University, Wuhan 430030, China.</p>	<p>RAT</p> <p>Abstract</p>	<p>The results showed that the degree of DNA damage in the fluoride group and the selenium group were significantly greater than that in control group(P < 0.01). The damage in the fluoride group was even more serious.</p> <p>It suggested that fluoride and selenium could induce DNA damage in pallium neural cells of rats respectively. Moreover, the joint antagonistic effect of selenium and zinc against fluoride was more obvious.</p> <p>Definition of Pallium: - the central cortex with the subajacent white substance.</p>
<p>Continued ...</p>		

<p>Chinese Journal of Endemiology 2000;19(4):262-3</p> <p>As cited and abstracted in Fluoride 2001; 34(1):80</p> <p>Effects of high fluoride drinking water on the cerebral functions of mice</p> <p>Sun Z-R, Liu F-Z, Wu L-N, et al.</p> <p>Dept. of Environmental Health, Tianjin Medical University, Tianjin 300070, China.</p>	<p>MOUSE</p>	<p>Results: Learning and memory abilities of high-fluoride exposed groups were significantly lower than that of the control group, while the brain ChE activities of high-fluoride exposed groups were significantly higher.</p> <p>Conclusions: High fluoride concentration in drinking water can decrease the cerebral functions of mice. Fluoride is a neurotoxicant</p>
<p>Chinese Journal of Endemiology 2000;19(2):96-8</p> <p>As cited and abstracted in Fluoride 2001; 34(1):82</p> <p>Study of the mechanism of neurone apoptosis in rats from the chronic fluorosis</p> <p>Lu X-H, Li G-S, Sun B</p> <p>Institute of Endemic Diseases in Norman Bethune University of Medical Sciences, Changchun, China</p>	<p>RAT</p>	<p>Conclusions: There is a tendency for neurone apoptosis in chronic fluorosis in rats. It is most evident with changes in pathology. It is not likely that only one form of neurone damage exist in the process of chronic fluorosis. There are recessive changes and apoptosis in the process at the same time.</p>
<p>Fluoride 2000. Vol. 33 No. 1:17-26.</p> <p>Effects of fluoride accumulation on some enzymes of brain and gastrocnemius muscle of mice</p> <p>M Lakshmi Vani and K Pratap Reddy</p>	<p>MOUSE</p> <p>NaF (20mg/kg/body weight) for 14 days</p> <p>FULL STUDY</p>	<p>Fluoride levels were significantly increased ($p < 0.01$) in both brain and gastrocnemius muscle.</p> <p>This study therefore shows that both brain and muscle are affected by fluoride with inhibition of some enzymes associated with free-radical metabolism, energy production and transfer, membrane transport, and synaptic transmission, but with an enhanced activity of XOD.</p>
<p>Continued ...</p>		

<p>Zhonghua Yu Fang Yi Xue Za Zhi 2000 Nov;34(6):330-2</p> <p>[Influence of free radical inducer on the level of oxidative stress in brain of rats with fluorosis]</p> <p>Shao Q, Wang Y, Guan Z.</p> <p>Dept. of Neurology, Guiyang Medical College, Guizhou 550004, China.</p>	<p>RAT</p> <p>Abstract</p>	<p>CONCLUSION: Over uptake of fluoride for a long term could cause potential increase in the level of oxidative stress in the brain tissue.</p>
<p>Wei Sheng Yan Jiu. 1999 Jul;28(4):210-2.</p> <p>[Effect of fluoride exposure on synaptic structure of brain areas related to learning-memory in mice]</p> <p>Zhang Z, Xu X, Shen X, Xu X.</p> <p>Department of Biology, Zhejiang Normal University, Jinhua 321004, China.</p>	<p>MOUSE</p> <p>NaF in drinking water</p> <p>Abstract</p>	<p>The learning-memory behavior was tested in mice on a Y-maze after drinking different concentration of sodium fluoride. The impairment on the structure of Gray 1 synaptic interface in the CA3 area of mice hippocampus were quantitatively analyzed by electron microscopy and computer image processing appliance. The main results are as follows: the learning ability of mice drinking high concentration of fluoride presented remarkable deterioration, the thickness of post-synaptic density (PSD) was decreased, and the width of synaptic cleft was remarkably increased. The results suggested that the impairment on the learning capability induced by fluorosis may be closely related with the pathological changes of synaptic structure in the brain of mice.</p>
<p>Arch Physiol Biochem. 1999 Feb;107(1):15-21.</p> <p>Fluoride enhances the effect of aluminium chloride on interconnections between aggregates of hippocampal neurons.</p> <p>van der Voet GB, Schijns O, de Wolff FA.</p> <p>Toxicology Laboratory Leiden University Medical Center Leiden, The Netherlands.</p>	<p><i>in vitro</i> system of cultured hippocampal neurons from foetal rats</p> <p>Abstract</p>	<p>It was concluded that aluminium interferes with the metabolism of the neuronal cytoskeleton and that this interference is potentiated by fluoride.</p>

<p>Neurotoxicol Teratol 1998 Sep-Oct;20(5):537-42</p> <p>Influence of chronic fluorosis on membrane lipids in rat brain.</p> <p>Guan ZZ, Wang YN, Xiao KQ, Dai DY, Chen YH, Liu JL, Sindelar P, Dallner G.</p> <p>Dept. of Pathology, Guiyang Medical College, Guizhou, China.</p>	<p>RAT</p> <p>30 or 100 ppm F for 3, 5, and 7 months.</p> <p>Abstract</p>	<p>The results demonstrate that the contents of phospholipid and ubiquinone are modified in brains affected by chronic fluorosis and these changes of membrane lipids could be involved in the pathogenesis of this disease.</p>
<p>Biomed Environ Sci 1998 Mar;11(1):1-6</p> <p>Actions of sodium fluoride on acetylcholinesterase activities in rats.</p> <p>Zhao XL, Wu JH.</p> <p>Dept. of Environmental Toxicology, Chinese Academy of Preventive Medicine, Beijing, China.</p>	<p>RAT</p> <p>pregnant rats ingested ad libitum fluorinated drinking water (5, 15, 50 ppm F-) during gestation and lactation</p> <p>Abstract</p>	<p>It was shown that the AChE activities of the SPM and peripheral RBCs in maternal rats exposed 5-50 ppm F- for 60 days were elevated significantly by 30.0-67.6% and 12.5-31.9% in a dose-dependent manner, respectively. The AChE activities of their offspring 80 days after birth were also increased (8.7-28.7% for SPM and 20.6-32.4% for RBC).</p>
<p>Brain Res 1998 Feb 16;784(1-2):284-98</p> <p>Chronic administration of aluminum-fluoride or sodium-fluoride to rats in drinking water: alterations in neuronal and cerebrovascular integrity.</p> <p>Varner JA (a), Jensen KF (b), Horvath W (c), Isaacson RL (a)</p> <p>(a) Psychology Dept, Binghamton University, Binghamton, NY (b) Neurotoxicity Div., NHEERL, EPA, Research Triangle Park, NC (c) Chemistry Dept, Binghamton University</p>	<p>RAT</p> <p>27 Adult Male Long-Evans rats</p> <p>52-weeks</p> <p>1 treated group received 0.05 ppm AIF3</p> <p>2nd treated group received 2.1 ppm NaF</p> <p>Administered in doubly distilled, deionized drinking water (ddw)</p> <p>Controls received ddw</p> <p>Abstract</p> <p>FULL TEXT available at Science Direct.</p>	<p>In NaF treated rats:</p> <ul style="list-style-type: none"> • Beta amyloid plaques (the classic brain abnormality of Alzheimer's disease) • Increased levels of aluminum in the brain (an important component of the neurological damage in Alzheimer's). • Authors speculate that fluoride facilitates aluminum's crossing of the blood brain barrier. They state (page 295): "Both the AIF3 and NaF groups had increased brain Al levels relative to the controls. The Al level in the NaF group was double that of controls and the Al level in the AIF3 group was even greater. The Al detected in the controls and NaF groups is most likely due to the presence of this element in the rat chow... It is possible that the NaF-treated group was able to form some amount of a AIF3 also capable of becoming bioavailable."

<p>JOURNAL OF CELLULAR BIOCHEMISTRY; 69 (2). 1998. 221-231.</p> <p>Induction of stress response and differential expression of 70 kDa stress proteins by sodium fluoride in HeLa and rat brain tumor 9L cells.</p> <p>CHENG T.J., CHEN TM, CHEN CH, LAI YK</p> <p>Dep. Life Sci., Natl. Tsing Hua Univ., Hsinchu 30043, Taiwan.</p>	<p>RAT</p> <p>Abstract</p>	<p>NaF acts as a stress response inducer on HeLa and 9L rat brain tumor cells.</p>
<p>Environmental Toxicology and Pharmacology 1998; 6: 187-191.</p> <p>Effects of sodium fluoride on locomotor behavior and a few biochemical parameters in rats</p> <p>Vanaja Paul, P. Ekambaram, A.R. Jayakumar</p> <p>Department of Pharmacology and Environmental Toxicology, Dr A.L.M. Postgraduate Institute of Basic Medical Sciences, University of Madras, Taramani Chennai 600 113, India</p>	<p>RAT (adult female)</p> <p>NaF 20 or 40 mg:kg dose daily for 60 days</p>	<p>A suppression of spontaneous motor activity suggests that fluoride has, by a central action, inhibited motivation of these animals to exhibit locomotor behavior. A cholinergic mechanism through a change in the activity of acetylcholinesterase may not account for this effect, since NaF treatment did not alter the activity this enzyme in brain regions. However, an involvement of monoamines may be proposed in view of previously reported finding that excessive fluoride intake has decreased the concentrations of 5-hydroxyindoleacetic acid and increased that of norepinephrine in rat brain.</p>
<p>Zhonghua Yu Fang Yi Xue Za Zhi 1997 Nov;31(6):330-3</p> <p>[Changes of coenzyme Q content in brain tissues of rats with fluorosis]</p> <p>Wang Y, Guan Z, Xiao K.</p> <p>Dept. of Scientific Research, Guiyang Medical College.</p>	<p>RAT</p> <p>66.3 mg/L and 221 mg/L F-containing water for 3, 5, and 7 months</p> <p>Abstract</p>	<p>Coenzyme Q content of brain tissue in rats fed with fluorine-containing water decreased at early stage of fluorosis, but increased significantly at late stage. It is speculated that changes in content of coenzyme Q could correlate with changes in free radical levels induced by fluorine.</p>
<p>Continued ...</p>		

<p>Zhonghua Yi Xue Za Zhi 1997 Aug;77(8):592-6</p> <p>[Influence of experimental fluorosis on phospholipid content and fatty acid composition in rat brain]</p> <p>Guan Z, Wang Y, Xiao K.</p> <p>Guiyang Medical College.</p>	<p>RAT</p> <p>Wistar rats were fed with NaF until chronic fluorosis was induced</p> <p>Abstract</p>	<p>CONCLUSION: The metabolism of brain phospholipid might be interfered by fluoride accumulated in brain tissue, which is related with the degeneration of neuron. The changes of brain phospholipid could be involved in the pathogenesis of chronic fluorosis.</p>
<p>Annals of the New York Academy of Sciences 825 152-166 1997</p> <p>Toxin-induced blood vessel inclusions caused by the chronic administration of aluminum and sodium fluoride and their implications for dementia.</p> <p>Isaacson RL, Varner JA, Jensen KF.</p> <p>Department of Psychology, Binghamton University, New York 13902-6000, USA.</p>	<p>RAT</p> <p>NaF</p> <p>2.1 ppm in drinking water for 45 weeks</p>	<p>Elevated brain level of aluminum</p> <p>Neuronal abnormalities were observed in the NaF treated animals- especially in the deeper cell layers.</p> <p>Both the AIF- and NaF-treated animals had substantial numbers of argentophilic cells on Bielchowsky staining and these cells showed condensed Nissl substance with hematoxylin and eosin staining. The NaF treatment also produced distortions of cells and, in some rats, cell losses could be demonstrated in particular brain regions. Both AIF3 and NaF induced vascular inclusions, although of a different character: the AIF3 produced the Al-based particles and the NaF produced the IgM inclusions.</p>
<p>Exp Gerontol 1997 Jul-Oct;32(4-5):441-50</p> <p>Age-related changes in axonal transport.</p> <p>Frolkis VV, Tanin SA, Gorban YN.</p> <p>Institute of Gerontology, Academy of Medical Sciences of Ukraine, Ukraine.</p>	<p>NaF</p> <p>Abstract</p>	<p>Small doses of NaF accelerated axonal transport (AT), and this correlated with a rise in cAMP levels in ventral roots. High doses of sodium fluoride decelerated AT more markedly in old rats.</p> <p>Changes in AT could be an important mechanism of disordering the growth of neurons and innervated cells in old age.</p>
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<p>Neurosci Behav Physiol. 1998 Jul-Aug;28(4):392-6.</p> <p>Adenylate cyclase system of the rat striatum: regulatory properties and the effects of gangliosides.</p> <p>Plesneva SA, Nalivaeva NN, Zhuravin IA.</p> <p>I. M. Sechenov Institute of Evolutionary Physiology and Biochemistry, Russian Academy of Sciences, St. Petersburg, Russia.</p>	<p>RAT</p> <p>Abstract</p>	<p>The activity and regulatory properties of the adenylate cyclase system of the rat striatum were studied. Agents such as Gpp(NH)p, forskolin, and NaF were found to show classical in vitro stimulation of adenylate cyclase activity in the striatum membrane fraction.</p>
<p>Neurotoxicol Teratol. 1995 Mar-Apr;17(2):169-77.</p> <p>Neurotoxicity of sodium fluoride in rats</p> <p>Mullenix PJ (1,2), Denbesten PK (3), Schunior A (3), Kernan WJ (4)</p> <p>(1) Toxicology Dept., Forsyth Research Institute, Boston MA (2) Dept. of Radiation Oncology, Harvard Medical School, Boston MA (3) Dept. of Pediatric Dentistry, Eastman Dental Center, Rochester NY (4) Veterinary Diagnostic Laboratory, Iowa State University, Ames IA</p>	<p>RAT</p> <p>Behavior was tested in a computer pattern recognition system</p> <p>Abstract</p> <p>FULL TEXT available at Science Direct.</p>	<p>Prenatal weanling and adult exposures all caused sex- and dose-specific behavioral deficits with a common pattern.</p> <p>Males were most sensitive to prenatal day 17-19 exposure, while females were more sensitive to weanling and adult exposures. After weanling and adult exposures the severity of deficits increased with increasing F levels found in plasma and specific brain regions such as the hippocampus.</p>
<p>Fluoride 1994; 27(3):155-159</p> <p>Effect of long-term administration of fluoride on levels of protein, free amino acids and RNA in rabbit brain</p> <p>Shashi A, Singh JP, Thapar SP</p> <p>Department of Zoology, Punjabi University, Patiala 14702, India</p>	<p>RABBIT</p> <p>5, 10, 20, and 50 mg/kg body wt/day by subcutaneous injection for 100 days</p>	<p>In fluoride treated rabbits the brain showed significant decline (P <0.001) in soluble, basic total protein and free amino acid levels. RNA content rapidly decreased (P <0.001) in the brains of experimental animals compared to the controls. However, in male animals treated with 5 and 10 mg fluoride no statistically significant differences in RNA content of brain were observed. The depletion of proteins produced degenerative changes in purkinje cells of the cerebellar cortex.</p>

<p>Zhonghua Yu Fang Yi Xue Za Zhi 1994 Sep;28(5):264-6</p> <p>[Effects of sodium fluoride on the activity of Ca²⁺Mg(2+)-ATPase in synaptic membrane in rat brain].</p> <p>Zhao XL, Gao WH, Zhao ZL.</p> <p>Department of Environment Health Ningxia Medical College, Yinchuan.</p>	<p>RAT</p> <p>Effects of NaF on Ca²⁺Mg(2+)-ATPase activity of synaptic membrane in rat brain were studied with <i>in vitro</i> or <i>in vivo</i> methods.</p> <p>Abstract</p>	<p>Concentrations of NaF of 0.3, 1.6, 8.0, 20.0 and 40.0 mmol/L can significantly inhibit the activity of the enzyme with proportions of 6.6%, 18.0%, 41.0%, 55.5% and 63.1%, respectively, and with a half inhibitory concentration of 14.8 mmol/L reflecting an obvious dose-effect and time effect relationship. Analysis of enzyme substrate kinetics showed the effect that NaF had was a non competitive inhibition. Activity of Ca²⁺Mg(2+)-ATPase on synaptic membrane in female rat brain showed a decreasing tendency after feeding with water fluorinated with 5, 15 and 50 mg/L of fluoride during their gestation and lactation for 50 days, and that in their newborn offsprings with 5 and 50 mg/L of fluoride was inhibited by 11.3 and 32.1%, respectively.</p>
<p>Hua Hsi I Ko Ta Hsueh Hsueh Pao. 25(2):188-91.1994</p> <p>[Effect of excessive fluoride intake on mental work capacity of children and a preliminary study of its mechanism]</p> <p>Li Y, Li X, Wei S</p>	<p>CHILDREN (12-13 years in endemic fluorosis area)</p> <p>RAT</p> <p>Abstract</p>	<p>(3) Excessive fluoride intake decreased 5-hydroxy indole acetic acid and increased norepinephrine in rat brain</p>
<p>Zhonghua Bing Li Xue Za Zhi 1992 Aug;21(4):218-20</p> <p>[The effect of fluorine on the developing human brain]</p> <p>Du L.</p> <p>Department of Pathology, Guiyang Medical College.</p>	<p>HUMAN Fetuses</p> <p>15 aborted fetuses at 5-8th gestation month from an endemic fluorosis area compared with those from a non-endemic area,</p> <p>Abstract</p>	<p>Stereological study of the brains showed that the numerical density of volume of the neurons and the undifferentiated neuroblasts as well as the nucleus-cytoplasm ratio of the neurons were increased. The mean volume of the neurons was reduced. The numerical density of volume, the volume density and the surface density of the mitochondria were significantly reduced. The results showed that chronic fluorosis in the course of intrauterine fetal life may produce certain harmful effects on the developing brain of the fetus.</p>

<p>Fluoride 1992; 25(2):77-84</p> <p>Studies on alterations in brain lipid metabolism following experimental fluorosis</p> <p>A Shashi</p> <p>Department of Zoology, Punjabi University, Patala 147002, India</p>	<p>RABBIT</p> <p>NaF at 5, 10, 20 and 50 mg/kg BW/day was injected subcutaneously for 100 days</p>	<p>Biochemical studies showed hyperlipidemia, hyperphospholipidemia, and hypertriglyceridemia in the brain of treated animals of both sexes.</p> <p>Fluoride exerts an inhibitory effect on the free fatty acids in brain of both sexes. The relevance of these results in experimental fluorosis is discussed.</p>
<p>Res 1992 Jun 26;583(1-2):155-60</p> <p>Beta-adrenergic receptor activity of cerebral microvessels in experimental diabetes mellitus.</p> <p>Mooradian AD, Scarpace PJ.</p> <p>St. Louis DVA Medical Center, MO.</p>	<p>RAT</p> <p>streptozotocin induced diabetic rats after 5 weeks of induction of diabetes</p> <p>Abstract</p>	<p>The net NaF stimulated AC activity in diabetic rats (109.5 +/- 11.4) was significantly lower than the control rats (154.3 +/- 16.3) (P less than 0.05).</p> <p>It is concluded that diabetes mellitus in rats is associated with reduced post receptor activation of adenylate cyclase in cerebral microvessels</p>
<p>ACTA PHYSIOL SIN; 43 (5). 1991. 512-517.</p> <p>An experimental study of inhibition on lactation in fluorosis rats.</p> <p>YUAN S-D, SON K-Q, XIE Q-W, LU F-Y</p> <p>Neuroendocrine Research Laboratory, China Medical University, Shenyang.</p>	<p>RAT (Lactating)</p> <p>Abstract</p>	<p>2) During chronic fluorosis serum PRL level was decreased, however, PRL content in pituitary was increased.</p> <p>Electronmicroscopic examination showed accumulation of large mature secretory granules and appearance of extremely large abnormal secretory granules in lactotroph cytoplasm.</p> <p>These finding indicate that hormone release of pituitary lactotrophs is obstructed in lactating rats with fluorosis, and the toxic effect of fluoride is mediated by an enhanced function of dopaminergic system in hypothalamus.</p>
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<p>CHIN J PREV MED; 25 (5). 1991. 269-271.</p> <p>The clinical features of 160 cases of acute sodium silico fluoride poisoning.</p> <p>Dong Y et al.</p> <p>First People's Hosp., Wenling County, Zhejiang 317500</p>	<p>HUMAN</p>	<p>160 cases of acute sodium silicofluoride poisoning due to accidental intake are reported in this paper... The cardiovascular findings were notable. Ninety-six cases had abnormal electrocardiographic findings. Abnormal heart rhythm and S-T segment changes were the main findings. These changes were positively correlated with the toxin amount of fluoride. Two cases died from sudden arrest of heart beat. Lung, kidney, liver, and brain functions were also impaired.</p>
<p>Biochem J 1990 Jun 15;268(3):733-7</p> <p>Dual effect of fluoride on phosphoinositide metabolism in rat brain cortex. Stimulation of phospholipase C and inhibition of polyphosphoinositide synthesis.</p> <p>Claro E, Wallace MA, Fain JN.</p> <p>Department of Biochemistry, University of Tennessee, Memphis 38163.</p>	<p>Abstract</p>	<p>under conditions where breakdown of polyphosphoinositides by phospholipase C was dependent on PtdIns kinase activity, fluoride inhibited activation by GTP[S] plus carbachol of phospholipase C. When conditions allowed direct breakdown of PtdIns and precluded PtdIns kinase activity, the stimulatory effects of fluoride and GTP[S] plus carbachol on phospholipase C activity were additive.</p>
<p>Zhonghua Bing Li Xue Za Zhi 1989 Dec;18(4):290-2</p> <p>[Experimental study of behavior and cerebral morphology of rat pups generated by fluorotic female rat]</p> <p>Liu WX.</p>	<p>RAT</p> <p>33-42-day old rat pups generated by three groups of female Wistar rats, which were given distilled water containing 0, 30 and 60 ppm NaF respectively beforehand as drinking water for 85 days</p> <p>Abstract</p>	<p>The results of behavior test showed that the latent period of pain reaction and that of conditioned reflex in the 30 ppm F and 60 ppm F groups were longer than that in the control group (P less than 0.05 or P less than 0.01). morphological examination of the pup brains showed that the nerve cell density of the 60 ppm F group was higher than that of the control group (P less than 0.05). Electronmicroscopically, mild degeneration of organelles of the nerve cells was observed in those brains of the 60 ppm F group.</p>
<p>Continued ...</p>		

<p>Shikwa Gakuho 1989 Mar;89(3):607-26</p> <p>[The rabbit thermo-regulatory system. Effects of high dose of sodium fluoride]</p> <p>Machida H.</p> <p>Article in Japanese.</p>	<p>RABBIT</p> <p>Abstract</p>	<p>The mechanism of NaF induced hypothermia was investigated on relations between the monoamine synthesis and metabolism in the rabbit brain.</p> <p>Administration of NaF made a significant decrease in norepinephrine levels in the rabbit hypothalamus, but had no effect on 5-HT levels.</p>
<p>Fluoride 1986; V 19, No 3: 108-112</p> <p>Kenetics of fluoride penetration in liver and brain</p> <p>Geeraerts F, Gijs G, Finne E, Crokaert R</p> <p>Department of Biochemistry and Pharmacology, Vrije Universiteit, Laarbeeklaan, Brussels, Belgium.</p>	<p>RAT</p>	<p>The blood-brain barrier fails to exclude the fluoride ion from nerve tissue.</p> <p>Fluoride levels in brain reach a maximum approximately two hours after it has been administered.</p>
<p>Zhonghua Bing Li Xue Za Zhi 1986 Dec;15(4):297-9</p> <p>[Morphology of the brain of the offspring of rats with chronic fluorosis]</p> <p>Guan ZZ.</p>	<p>RAT</p>	<p>No Abstract available</p>
<p>Acta Physiol Pol 1984 May-Jun;35(3):199-206</p> <p>Effect of certain agents on subcellular cAMP level in different areas of rat brain.</p> <p>Janiszewska G, Lachowicz L, Wojtkowiak R.</p>	<p>RAT</p> <p>Abstract</p>	<p>The influence was studied in vitro of certain agents (adenosine, ADP, ATP, theophylline, together with F- ions) on the cAMP concentrations in the nuclear (N) and mitochondrial (M) fractions from different areas of rat brain. F- ions caused a slight decrease of the cAMP concentrations in nuclear fractions of the thalamus with hypothalamus and a marked decrease of this cyclic nucleotide in M fractions from the cerebral cortex.</p>
<p>Continued ...</p>		

<p>Int J Clin Pharmacol Ther Toxicol. 1982 Jul;20(7):334-8.</p> <p>Accidental ingestion of NaF tablets by children--report of a poison control center and one case.</p> <p>Eichler HG, Lenz K, Fuhrmann M, Hruby K.</p>	<p>CHILD</p> <p>Accidental ingestion of NaF tablets</p> <p>a 3-year-old boy who swallowed 200 NaF tablets (1 mg fluoride each) for a dose of 16 mg fluoride/kg body weight</p> <p>Abstract</p>	<p>The boy died 7 hours after fluoride ingestion. Upon autopsy, hemorrhagic edema of the lungs, hemorrhagic gastritis, and massive cerebral edema were observed.</p>
<p>J TOKYO MED COLL; 39 (3). 1981. 441-460.</p> <p>Hygienic study on fluoride: 4. Physiological effects of fluoride on rat.</p> <p>Tomomatsu T</p> <p>Dep. Biochem., Tokyo Med. Coll.</p> <p>Toxline abstract available at Toxnet</p>	<p>RAT</p> <p>The effects of fluoride (F-) administration were studied on 2 groups of weanling male Wistar rats, a control fed a basal diet containing 0.09 mg% F- and the other fed a diet containing 50 mg% F- for 30 days.</p>	<p>The amount of F- accumulated in brain, heart, thymus, kidney, testes, adrenal and femur of the F--fed group was significantly higher than those of controls.</p>
<p>Morb. Mortal. Wkly. Rep.; VOL 29 ISS Mar 28 1980, P134-136</p> <p>Fluoride intoxication in a dialysis unit--Maryland</p> <p>Anderson R, Beard JH, Sorley D</p> <p>Bureau of State Services, and the Chronic Diseases Div., Field Services Div., Bureau of Epidemiology, Cent. for Disease Control, Atlanta, GA 30333</p>	<p>HUMAN</p>	<p>Case reports are presented of 8 patients with end stage renal disease who while undergoing dialysis received IV, excessive amounts of fluoride due to an unreported spill of hydrofluosilicic acid into the public water supply caused by cross connections in a treatment plant...</p> <p>One patient upon autopsy was found to have high fluoride levels in lung tissue (5.6 ppm), kidney (7.0 ppm), brain (0.9 ppm) and blood (4.9 ppm).</p>
<p>FLUORIDE; 12 (3). 1978 111-114</p> <p>Nonskeletal fluorosis.</p> <p>Anon</p>	<p>A wide variety of symptoms are encountered in chronic (human, animal) fluorosis. The soft tissue organs affected by F- are named in the following order: aorta, thyroid gland, lungs, kidneys, heart, pancreas, brain, spleen and liver. With advancing age their F- content increases.</p> <p>Inhalation of fluoride produces foci of demyelination in the cortex and in subcortical areas and a decrease in the number of Purkinje cells in the cerebellum.</p>	
<p>Continued ...</p>		

<p>Folia Histochem Cytochem (Krakow) 1974;12(1):37-44</p> <p>Histochemical studies on the effect of sodium fluoride on metabolism in Purkinje's cells.</p> <p>Czechowicz K, Osada A, Slesak B.</p>	<p>GUINEA PIG</p> <p>Toxline abstract available at Toxnet</p>	<p>The effect of prolonged administration of NaF on the metabolism of (guinea pig) Purkinje cells in the cerebellar cortex was studied by histochemical methods. Experimentation showed an intensification of the metabolic activity of the mitochondria and probably of the membrane system of the endoplasmic reticulum, activation of the complex of enzymes connected with active transport through membrane structures of cells and the absence of perceptible changes in the process of protein synthesis in experimental animals as compared with controls.</p>
<p>GIG TR PROF ZABOL; (5). 1974 25-27</p> <p>Aspects of nervous system affections in occupational fluorosis.</p> <p>POPOV LI, FILATOVA RI, SHERSHEVER AS</p>	<p>FLUOROSIS PATIENTS</p> <p>Toxline abstract available at Toxnet</p>	<p>Neurological symptomatology in the form of the syndrome of vegetative-vascular dysfunction, or the asthenovegetative syndrome with polyneuritic (sensory and vegetative) disorders was detected in 78.8% of patients with occupational fluorosis in preosteal and osteal stages. Clinical and physiological investigations of the nervous system (psycho-physiological procedures, EEG, chronaximetry) showed patients with fluorosis to exhibit disturbed higher nervous activity and dysfunction of subcorticalaxial nonspecific structures of the brain.</p>
<p>J Biol Chem 2003. Apr 3</p> <p>Atypical effect of salts on the thermodynamic stability of human prion protein</p> <p>Apetri AC, Surewicz WK.</p> <p>Physiology and Biophysics, Case Western Reserve University, Cleveland, OH 44106.</p>	<p>HUMAN PRION PROTEIN</p> <p>Chemical unfolding studies in urea show that at low concentrations (below approximately 50 mM), all salts tested (sodium sulfate, sodium fluoride, sodium acetate and sodium chloride) significantly reduce the thermodynamic stability of the protein.</p> <p>no other protein has been reported to be destabilized by kosmotropes such as fluoride, sulfate or acetate. Therefore, the present finding points to rather unique properties of the prion protein.</p> <p>The present data indicate that electrostatic interactions play an</p>	

	unusually important role in the stability of the prion protein. FULL STUDY
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