

slightly. In arterioles it dropped only 8% on average. The hemodynamic response of individual arterioles was heterogeneous, probably due to the mesenteric angioarchitectonics. The polymer lowered blood pressure in radial arteries by 19.4 and 18.4% (in comparison with the period before and after administration of adenosine, respectively); AP dropped by 10.3%; the pressure in arterioles dropped by 23.6 and 17.1%, respectively (AP by 14.3%).

As is seen from a comparison of Tables 1 and 4, there are no essential differences in the hemodynamic effect of the polymer on the native and adenosine-dilated arterioles.

The obtained results are in conformity with a previous report [4] that polymers in the circulation primarily affect the microdisturbances caused by movement of the formed elements of the blood. In other words, similarly to the case with rigid tubes [3], it is the changes in the flow pattern rather than dilation of the resistive vessels which determine both the macro- and microhemodynamic effect of the polymer. Moreover, according to the data reported here, the contribution of this

purely flow pattern-dependent component in the resistance of arterioles may be considerable.

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# Morphochemical Manifestations of Chronic Exposure of the Brain to Amphetamine and Their Correction by Delta-Sleep Peptide

L. M. Gershtein, A. V. Sergutina,  
and V. I. Rakhmanova

UDC 612.82.018:577.175.523].019.08

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 116, № 11, pp. 555-557, November, 1993  
Original article submitted April 27, 1993

**Key Words:** *amphetamine; rat brain neurons; structured proteins; aminopeptidase*

The present investigation was aimed at determining the specificity of the morphochemical response of some brain structures to injections of amphetamine, a known psychotropic drug, and at correct-

ing amphetamine-induced changes with the use of delta-sleep peptide (DSP).

## MATERIALS AND METHODS

Experimental data were obtained using 4 groups of Wistar rats weighing 200-250 g.

Research Institute of the Brain, Russian Academy of Medical Sciences, Moscow. (Presented by O. S. Adrianov, Member of the Russian Academy of Medical Sciences)

TABLE 1. Interferometric Determination of Protein Content and Concentration (Dry Weight of Compact Substances) for a Single Injection of Amphetamine ( $M \pm m$ )

Parameter	Sensorimotor cortex				Caudate nucleus	
	layer III		layer V			
	control	amphetamine, single injection	control	amphetamine, single injection	control	amphetamine, single injection
Area, $\mu^2$	41.30 $\pm$ 0.53	50.68 $\pm$ 0.83 (122.8)	165.66 $\pm$ 1.96	151.59 $\pm$ 2.72 (91.5)	32.86 $\pm$ 0.49	33.67 $\pm$ 0.54 (102.4)
Protein content, pg	30.23 $\pm$ 0.68	47.14 $\pm$ 0.91 (160)	149.93 $\pm$ 2.64	155.79 $\pm$ 4.11 (103.9)	23.05 $\pm$ 0.45	30.73 $\pm$ 0.72 (133.5)
Protein concentration, pg/ $\mu^3$	0.72 $\pm$ 0.01	0.93 $\pm$ 0.01 (129.2)	0.90 $\pm$ 0.01	1.02 $\pm$ 0.01 (113.3)	0.70 $\pm$ 0.01	0.91 $\pm$ 0.01 (130)
Area, $\mu^2$	50.89 $\pm$ 0.59	49.03 $\pm$ 0.70 (96.3)	108.39 $\pm$ 1.34	104.70 $\pm$ 1.74 (96.6)	42.88 $\pm$ 0.44	42.17 $\pm$ 0.48 (98.3)
Protein content, pg	20.76 $\pm$ 0.50	24.33 $\pm$ 0.69 (117.2)	51.90 $\pm$ 1.06	58.16 $\pm$ 1.68 (112.1)	16.25 $\pm$ 0.33	22.05 $\pm$ 0.61 (135.4)
Protein concentration, pg/ $\mu^3$	0.41 $\pm$ 0.01	0.50 $\pm$ 0.01 (121.9)	0.48 $\pm$ 0.01	0.56 $\pm$ 0.01 (116.7)	0.38 $\pm$ 0.01	0.52 $\pm$ 0.01 (136.8)

Note. Here and in Tables 2 and 3: numbers in parentheses show percentage vs. control (100%).

Group I was the control; group II comprised animals which received a single intraperitoneal dose of amphetamine (2.5 mg/kg); group III comprised animals chronically given amphetamine (2.5 mg/kg, daily); group IV animals were injected with DSP (60  $\mu$ g/kg, daily) for 3 days before being sacrificed, against the background of chronic administration of amphetamine.

Sixty minutes after the last injection the animals were euthanized by air embolism; the brain was fixed in Carnoy's fluid, and histological preparation was performed in accordance with the routine cytochemical procedure [3]. The brain,

embedded in paraffin, was cut into sections 7  $\mu$  thick.

The dry weight of compact substances, which reflects the content and concentration of structured proteins in the neurons, was interferometrically determined in the cytoplasm and nuclei of the neurons [1]. Simultaneously, the profile fields of the nuclei and cytoplasm of neurons were measured using an MOB 1-15 ocular-micrometer. Sections stained with cresyl-violet after Viktorov [2] served as the morphological control. The activity of one of the enzymes of protein catabolism, aminopeptidase (AMP), was cytochemically quantitated on a

TABLE 2. Interferometric Determination of Protein Content and Concentration (Dry Weight of Compact Substances) for Chronic Administration of Amphetamine ( $M \pm m$ )

Parameter	Sensorimotor cortex						Caudate nucleus		
	layer III			layer V					
	control	amphetamine, chronic injection	amphetamine + 3 injections of DSP	control	amphetamine, chronic injection	amphetamine + 3 injections of DSP	control	amphetamine, chronic injection	amphetamine + 3 injections of DSP
Cytoplasm									
Area, $\mu^2$	41.30 $\pm$ 0.53	48.37 $\pm$ 1.23 (117.2)	49.68 $\pm$ 0.77 (120)	165.66 $\pm$ 1.96	144.09 $\pm$ 2.46 (86.9)	152.10 $\pm$ 2.32 (91.8)	32.86 $\pm$ 0.49	31.10 $\pm$ 0.45 (94.5)	28.92 $\pm$ 0.32 (87.8)
Protein content, pg	30.23 $\pm$ 0.68	39.56 $\pm$ 1.07 (131.1)	38.85 $\pm$ 1.08 (128)	149.93 $\pm$ 2.64	127.66 $\pm$ 4.41 (85.1)	124.62 $\pm$ 2.32 (83.1)	23.05 $\pm$ 0.45 (110.3)	25.37 $\pm$ 0.51 (87.8)	20.80 $\pm$ 0.32
Protein concentration, pg/ $\mu^3$	0.72 $\pm$ 0.01 (115.3)	0.83 $\pm$ 0.13 (107)	0.77 $\pm$ 0.01	0.90 $\pm$ 0.01 (98.9)	0.89 $\pm$ 0.02 (91.1)	0.82 $\pm$ 0.01	0.70 $\pm$ 0.01 (115.7)	0.81 $\pm$ 0.01 (102.8)	0.72 $\pm$ 0.01
Nucleus									
Area, $\mu^2$	50.89 $\pm$ 0.59	47.63 $\pm$ 0.56 (93.6)	51.07 $\pm$ 0.80 (100)	108.39 $\pm$ 1.34	97.02 $\pm$ 1.17 (89.5)	116.27 $\pm$ 1.52 (107.3)	42.88 $\pm$ 0.44	41.01 $\pm$ 0.42 (95.6)	37.99 $\pm$ 0.45 (88.8)
Protein content, pg	20.75 $\pm$ 0.50	21.48 $\pm$ 0.47 (103.5)	22.94 $\pm$ 0.75 (110.5)	51.90 $\pm$ 1.06	43.79 $\pm$ 1.14 (84.4)	52.06 $\pm$ 0.94 (100.4)	16.25 $\pm$ 0.33	18.42 $\pm$ 0.42 (113.4)	15.95 $\pm$ 0.47 (98.15)
Protein concentration, pg/ $\mu^3$	0.41 $\pm$ 0.01	0.45 $\pm$ 0.01 (109.7)	0.44 $\pm$ 0.01 (107.3)	0.48 $\pm$ 0.01	0.45 $\pm$ 0.01 (93.7)	0.45 $\pm$ 0.01 (93.7)	0.38 $\pm$ 0.01	0.45 $\pm$ 0.01 (118.4)	0.42 $\pm$ 0.01 (110.5)

TABLE 3. Activity of Amino-peptidase for Single and Chronic Administration of Amphetamine

Brain structures	Control	Amphetamine, single injection	Amphetamine, chronic injection	Amphetamine + 3 injections of DSP
Layer III of sensorimotor cortex	0.366±0.02	0.401±0.006 (109.6)	0.365±0.003 (99.7)	0.346±0.003 (94.5)
Layer V of sensorimotor cortex	0.522±0.003	0.578±0.007 (110.7)	0.534±0.002 (102.3)	0.521±0.007 (99.8)
Caudate nucleus	0.426±0.003 (115.7)	0.493±0.005 (94.6)	0.403±0.005 (94.8)	0.404±0.003
<i>n. accumbens</i>	0.445±0.005	0.546±0.006 (122.7)	0.432±0.004 (97.1)	0.419±0.003 (94.2)
Hippocampus	0.467±0.003	0.459±0.006 (93.8)	0.493±0.004 (94.4)	0.450±0.004 (96.3)

LYUMAM-IZ microscope in 20-μ thick sections prepared on a cryotome [4]. The cortico-subcortical (layers III and V of the sensorimotor cortex and the caudate nucleus) structures of the locomotor system and some structures in the limbic (hippocampus) and mesolimbic (*n. accumbens*) systems were examined. The experimental results were processed using computer software.

## RESULTS

After a single injection of amphetamine, the protein content and concentration, as well as the dimensions of the cytoplasm (only in layer III of the sensorimotor cortex), reliably increased. At the same time, a reliable increase in the dry weight and concentration of proteins was noted in the nuclei of neurons of all the structures examined, whereas the size of neurons remained virtually unchanged versus that in the control animals (Table 1).

Simultaneously, the activity of AMP increased in the neurons of the sensorimotor cortex, caudate nucleus, and *n. accumbens* (Table 3).

Chronic administration of amphetamine gave rise to a complicated picture of changes in the morphochemical parameters. As in the case of a single injection, the strongest activation-type response was observed in the cytoplasm of layer III neurons. In the neurons of layer V, deficiency-type changes were noted, whereas in the caudate nucleus a diminution of the neurocyte cytoplasm was attended by an increase in the protein content and concentration (Table 2). The AMP activity in the neurons of the structures under investigation was virtually at the same level as in the control animals (Table 3).

Against the background of chronic administration of amphetamine, thrice repeated injections of

DSP to a certain extent, but not entirely, normalized the morphochemical shifts in layer III of the sensorimotor cortex, whereas in layer V and the caudate nucleus, where the neurocyte size tended to drop vs. the control, normalization of the protein content and concentration was not revealed (Table 2). No reliable differences were noted between the AMP activity after DSP administration and in the control (Table 3).

Thus, definite morphochemical differences were discovered between the responses of the brain structures examined. Such differences were apparent for diverse morphofunctional types of neurons in the sensorimotor cortex (neurons of layers III and V), as well as for neurons in the cortico-subcortical structures. Our findings are confirmed by studies performed by neurophysiologists who established that it is typical of chronically administered phenamine that the intensity of cell reactions in the locomotor cortex and caudate nuclei (with certain differences in the responses of neurons in these structures) markedly exceed the normal level [5]. The results obtained on this model are also corroborated by the DSP correction of the effect of amphetamine, which manifested itself in various degrees of normalization of amphetamine-induced changes.

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