BIOPHYSICS AND BIOCHEMISTRY

Neurochemical Characteristics of the Effects of Delta Sleep-Inducing Peptide in Wistar Rats with Hyperactivity of the Dopaminergic System

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Quantitative cytochemical assay showed that single injection of delta sleep-inducing peptide increased monoamine oxidase activity (substrates: serotonin and tryptamine) in the caudate and accumbens nuclei and glutamate dehydrogenase activity in the hippocampus of stress-resistant Wistar rats chronically treated with L-DOPA. Enzyme activities in the sensorimotor cortex did not change. Delta sleep-inducing peptide had no effects on acetylcholine esterase and aminopeptidase activities in the brain of Wistar rats.

Key Words: *Wistar rats; brain; L-DOPA; delta sleep-inducing peptide; enzyme activity; protein and neurotransmitter metabolism*

Neuropeptides regulating animal behavior are widely used in neurochemistry for studying the responses of various brain structures and metabolic systems.

Delta sleep-inducing peptide (DSIP) modulates activity of the central neurotransmitter systems, including the serotoninergic system [5].

The effects of DSIP on the brain in stress-resistant Wistar rats displaying less pronounced L-DOPA-induced morphochemical changes than stress-sensitive August rats are of particular interest [3]. Here we studied the effects of DSIP on brain structures responsible for the formation and realization of goal-directed behavior in Wistar rats with hyperactivity of the dopaminergic system induced by chronic administration of L-DOPA.

MATERIALS AND METHODS

Brain samples were taken from Wistar rats weighing 230 g and crossing 178±15.0 squares in the open field test over 5 min. Control animals were injected with physiological saline. Experimental rats were daily administered with L-DOPA (25.5 mg/kg Madopar-125 in physiological saline) for 2 weeks and then received single injection of 60 μg/kg DSIP. The animals were decapitated under light ether anesthesia. Cryostat sections (20 μ) of the sensorimotor cortex (layers III and V and areas FP^a, FP^p, and PA [2]), accumbens and caudate nuclei, and hippocampus (area CA3) were prepared. Activities of aminopeptidase (AMP) [1], glutamate dehydrogenase (GDG) [9], monoamine oxidase (MAO) [7] (separate measurements with substrates serotonin and tryptamine), and acetylcholine esterase (AChE) [8] were measured on a LUMAM-I3 microscope (Russia) at 589 (GDG and MAO), 550 (AMP), and 488 nm (AChE) and expressed in optical density units. The results were analyzed by Student's *t* test; 150 cells (GDG and AMP activities) or 150 filamentous structures (MAO and AChE activities) in each brain structure were analyzed in 3 control and 3 experimental rats.

RESULTS

DSIP increased MAO activity in the caudate and accumbens nuclei of rats treated with L-DOPA (substrate serotonin: by 14 and 21%, respectively; sub-

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TABLE 1. AChE and MAO Activities (Optical Density Units) in CNS of Wistar Rats Treated with L-DOPA and L-DOPA+DSIP (*M*±*m*)

Brain structure	AChE		MAO			
			substrate serotonin		substrate tryptamine	
	L-DOPA	+DSIP	L-DOPA	+DSIP	L-DOPA	+DSIP
Cortex						
layer III	0.382±0.002	0.407±0.003 (106.5)	0.338±0.003	0.365±0.002 (108.0)	0.384±0.003	0.373±0.002 (97.1)
layer V	0.558±0.004	0.599±0.003 (107.3)	0.497±0.003	0.515±0.002 (103.6)	0.491±0.002	0.493±0.002 (100.0)
Caudate nucleus	1.784±0.009	1.640±0.008 (91.9)	0.332±0.002	0.377±0.002 (113.6)*	0.305±0.002	0.355±0.002 (116.4)*
Accumbens nucleus	1.566±0.008	1.528±0.007 (97.6)	0.366±0.002	0.443±0.003 (121.0)*	0.361±0.003	0.399±0.002 (110.5)
Hippocampus	0.803±0.006	0.780±0.005 (97.2)	0.432±0.002	0.416±0.003 (96.3)	0.398±0.003	0.417±0.002 (104.8)

Note. Here and in Table 2: % of changes caused by L-DOPA alone is shown in brackets. *$p<0.05$ compared to parameters without DSIP.

strate tryptamine: by 16 and 21%, respectively, Table 1). No significant changes were found in the sensorimotor cortex and hippocampus. AChE activity did not differ from normal. At the same time, our previous studies showed that L-DOPA alone has no effects on MAO and AChE activities in brain structures [3].

DSIP had no effect on GDG activity in the sensorimotor cortex and subcortical nuclei in rats treated with L-DOPA (compared to L-DOPA-induced changes), but increased this activity in the hippocampus by 13%. AMP activity remained unchanged (Table 2). Chronic treatment with L-DOPA alone increased GDG activity in the caudate and accumbens nuclei (by 23 and 12%, respectively, compared to the control), but did not change this parameter in the sensorimotor cortex and hippocampus. AMP activity did not differ from normal [3].

Thus, DSIP abolished or attenuated L-DOPA-induced changes in enzyme activities in brain structures of stress-sensitive August rats [4]. By contrast, in Wistar rats DSIP increased GDG and MAO activities in the hippocampus and subcortical nuclei, respectively, but diminished L-DOPA-induced rise of GDG activity in subcortical nuclei.

Physiological studies showed that atypical afferent impulses to basal ganglia induced by L-DOPA are selectively blocked by DSIP [6]. DSIP produced no mor-

TABLE 2. Activities of Aminopeptidase (Optical Density Units) and Glutamate Dehydrogenase in CNS of Wistar Rats Treated with L-DOPA and L-DOPA+DSIP (*M*±*m*)

Brain structure	Aminopeptidase		Glutamate dehydrogenase	
	L-DOPA	+DSIP	L-DOPA	+DSIP
Cortex layer III	0.425±0.003	0.414±0.003 (97.4)	0.614±0.004	0.560±0.003 (91.2)
layer V	0.592±0.002	0.570±0.003 (96.3)	0.812±0.006	0.796±0.005 (98.0)
Caudate nucleus	0.537±0.003	0.563±0.003 (95.2)	0.934±0.006	0.856±0.008 (91.6)
Accumbens nucleus	0.571±0.004	0.574±0.002 (99.5)	0.942±0.008	0.894±0.008 (94.9)
Hippocampus	0.479±0.003	0.474±0.003 (99.0)	0.574±0.004	0.648±0.004 (112.9)*

phochemical changes in layers III (associative neurons) and V (efferent neurons) of the sensorimotor cortex. However, we revealed changes in the caudate (subcortical center of the motor system) and accumbens nuclei (transduction of motivation signals to the motor system) and hippocampus (limbic system), which correlated with the physiological state of animals.

Thus, DSIP regulates the central nervous system (CNS) in stress-resistant Wistar rats and stress-sensitive August rats [4] treated with L-DOPA. However, morphofunctional reactions to DSIP differed in these animals.

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