EFFECT OF DELTA SLEEP-INDUCING PEPTIDE ON DEVELOPMENT OF TOXIC CEREBRAL EDEMA AND SWELLING

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KEY WORDS: cerebral edema and swelling; delta sleep-inducing peptide

Delta sleep-inducing peptide (DSIP) modifies the activity of certain neurotransmitter systems of the brain, including adrenergic, serotoninergic, cholinergic, and GABA-ergic [1]. It was shown previously that these systems are involved in the pathogenesis of cerebral edema and swelling (CES) [6].

The aim of this investigation was to study the effect of DSIP on the development of CES.

EXPERIMENTAL METHOD

Toxic (nicotine-induced) CES was produced in Wistar rats weighing 140-180 g and its development was assessed by determining the moisture content and density of brain tissues from the left hemisphere, as described previously [5]. DSIP (synthesized at the M. M. Shemyakin Institute of Biological Chemistry, Russian Academy of Sciences) was injected intraperitoneally 1 h before intraperitoneal injection of nicotine in a dose of 40 μg/kg.

EXPERIMENTAL RESULTS

As Table 1 shows, DSIP in doses of 25 and 50 μg/kg did not affect the development of CES, but in doses of 75 and 100 μg/kg it had marked antiedema activity. With respect to the parameters studied, the brain tissues of animals of the control group and of rats receiving DSIP in dose of 75 μg/kg were virtually indistinguishable. Consequently, this was the optimal antiedema dose.

Conversely, DSIP in a dose of 200 μg/kg not only did not restore the normal moisture content and density of the brain tissues, but it exhibited synergism with the edematous factor (Table 1).

Moreover, worsening of the pathological process was observed macroscopically: the brain was anemic, jellylike, and friable.

TABLE 1. Effect of Delta Sleep-Inducing Peptide (DSIP) on Development of Toxic Cerebral Edema and Swelling (CES) (M ± m)

Experimental conditions	Number of rats	Total water content in brain tissue, %	Density of brain tissue, g/cm^3
Control	30	78,430±0,102	1,04280±0,00006
CES	30	79,570±0,175*	1,03790±0,00016*
CES + DSIP			
25 μg/kg	10	79,060±0,169*	1,03950±0,00272*
50 μg/kg	10	79,510±0,258*	1,03910±0,00291*
75 μg/kg	10	78,380±0,163*	1,04200±0,00103*
100 μg/kg	10	78,850±0,212**	1,04010±0,00494**
200 μg/kg	10	79,960±0,206*	1,03790±0,00272*

Legend. Significance of differences $p < 0.05$ (Student's test): *) with control, **) with CES.

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Thus DSIP acts in opposite ways on CES depending on its dose. This is in agreement with data in the literature: different doses of DSIP have opposite metabolic effects [3].

The antiedematous effect of drugs is known to take place through different mediator systems of the brain [6]. Meanwhile DSIP has well-marked neuromodulating properties [2, 4]. For that reason the mechanism of action of DSIP on CES is in all probability highly complex and multicomponent in nature. The possibility cannot be ruled out that the antiedematous effect of DSIP is realized through inhibition of the serotoninergic, adrenergic, and histaminergic systems and activation of GABA-ergic processes in the brain.

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EFFECT OF NEGATIVELY CHARGED LIPOSOMES ON ADP-INDUCED PLATELET AGGREGATION

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Platelet activation is accompanied by intensive transfer of phosphatidylserine, phosphatidylethanolamine, and phosphatidylinositol from the inner to the outer surface of the membranes [6]. This process correlates with the intensity of aggregation and procoagulant activity of the cells [5, 7, 11]. The appearance of additional amounts of phospholipids in the blood stream in the composition of liposomes can alter the functional state of the platelets and of the hemostasis system as a whole [1, 2, 8]. Some workers [9] studied the effect of liposomes of different composition on platelet aggregation and found that while they themselves did not cause aggregation, they modulated the response of the platelets to ADP. The effect of the liposomes depended on the charge on the lipid membrane. Neutral vesicles had no effect, whereas positively charged liposomes significantly inhibited ADP-induced aggregation in platelet-enriched plasma (PEP). Negatively charged liposomes did not affect the PEP-ADP system but inhibited aggregation of washed platelets in response to thrombin. The authors cited used phosphatidylglycerol as a negatively charged phospholipid.

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