sociated with its partial deposition in the intracellular space with subsequent release into circulation [6]. This is consistent with our observation that osmotic activity of Polyosm increases gradually, reaching the maximum 10-15 min after injection [8]. The finding that Polyosm induces no abrupt changes in SAP and CVP agrees with the data of others on the effects of polyethylene oxide 400 in glaucoma [5,9].

Our results indicate that Polyosm is a prospective preparation producing no side effects typical of osmotic diuretics.

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Postnatal Stress Impairs the Learning of Two-Way Avoidance Task in Prenatally Alcoholized Adult Rats

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Mild stress (handling and subcutaneous injection of 0.9% NaCl from postnatal day 8 through day 20) normally improves acquisition of a shuttle-box avoidance task in mature male rats. In the offspring of rats given intragastral injections of 25% ethanol (5 g/kg) from day 1 till day 20 of pregnancy, both handling and injections impair learning.

Key Words: *prenatal alcoholization; postnatal stress; bilateral avoidance; rats*

Environmental enrichment during early postnatal ontogeny, in particular handling, usually improves learning and increases the mass of the brain and especially of brain cortex in healthy mature animals, while environmental depletion during this period impairs behavioral capacity of the offspring [3,9]. On the other hand, in some cases mild stress caused by handling and injections impairs the higher nervous activity, for instance, the retrieval of passive avoidance task [6]. In light of this two questions arise: how stressful environental enrichment during early postnatal ontogeny affects the offspring with various disturbances of the central nervous system (CNS), for example, induced by prenatal alcoholization [4], and whether such environmental enrichment acts as therapeutic or pathogenic factor.

The aim of the present study was to examine the effect of environmental enrichment in the form of handling and injections in early postnatal ontogeny on learning in health and after prenatal alcoholization.

MATERIALS AND METHODS

The study was carried out on 16 random-bred albino rats. Each group comprised 4 litters. The rats of

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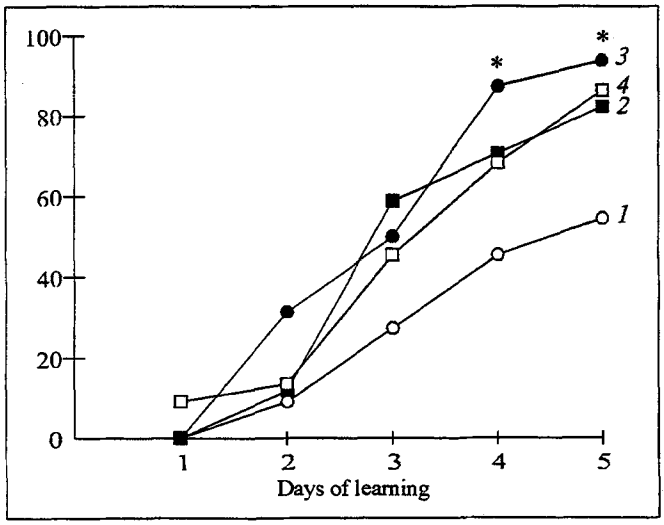

Fig. 1. Effect of prenatal alcoholization and postnatal handling and stress on acquisition of two-way avoidance task in adult rats. Ordinate: number of rats (%) attained acquisition criterion to the corresponding day of conditioning. *1*) prenatally alcoholized postnatally stressed animals; 2) prenatally alcoholized nonstressed rats; 3) nonalcoholized postnatally stressed offspring; *4*) nonalcoholized nonstressed offspring. *$p<0.05$ compared with group 1.

group 1 received 25% ethanol every day (5 g/kg, intragastrally) from day 1 till day of pregnancy 20, and their offspring were subcutaneously injected with 0.9% NaCl from day 8 till day 20 of postnatal life, i.e., the pups were subjected to stress in the form of handling and injections. Group 2 rats received ethanol (5 g/kg per day), but their offspring were not stressed until weaning (prenatally alcoholized nonstressed pups). Water was given intragastrally to group 3 rats during pregnancy (days 1-20), and their offspring were injected with 0.9% NaCl from day 8 till day 20 of postnatal development (nonalcoholized postnatally stressed pups). Group 4 rats were given water intragastrally during pregnancy, and their pups were not stressed until weaning (nonalcoholized nonstressed pups). On postnatal day 21, male pups were separated from female pups. At the age of 3 month, they were trained a two-way avoidance task (TWAT) in the Ugo Basile shuttle-box using sound as a stimulus. If the rat did not run into the opposite compartment within 4 sec after the sound was turned on, electrical current was delivered to the floor. The sound and current were turned off after 4 sec, if no transition was observed within that time. Fifty combinations of sound and aversive stimulation were presented every day. The rats were trained TWAT until they performed 8 avoidance responses per 10 presentations of the conditioning stimulus (acquisition criterion), but no longer than for 5 days. Acquisition of TWAT was evaluated by the number of rats (percent) attaining the acquisition criterion to each subsequent day of 5-day training. Statistical significance of the intergroup differences was evaluated using χ^2 test.

RESULTS

As seen from Fig. 1, adult males subjected to prenatal alcoholization and early postnatal stress (group 1) had the worst parameters of learning in the TWAT. The mean number of animals attaining the acquisition criterion on days 4 and 5 significantly differed from that observed in group 3 (nonalcoholized postnatally stressed rats). The nonstressed animals, whether alcoholized (group 2) or not (group 4), were intermediate in their ability to learn the TWAT between alcoholized and stressed (group 1) and nonalcoholized and stressed (group 3) offspring, so that these groups did not differ significantly from group 1 (although surpassed it by absolute values) and group 3.

These data (Table 1) suggest that mild stress in the form of handling and injections represents an environmental enrichment and promotes the development of CNS in healthy animals, judging from the TWAT parameters. Prenatal alcoholization inverted this effect, and handling and injections became a pathogenic factor. This seems to argue with the data of other investigators [10] on the ameliorating effect of environmental enrichment during early ontogeny in prenatally alcoholized rats. However, environmental stimulation in these experiments was performed from postnatal day 25 to 60, i.e., later than in our study. It can be hypothesized that the environmental enrichment without stress in rats during early ontogeny, which corresponds to the first weeks and months of postnatal development in men [7], can produce a positive effect on prenatally alcoholized offspring, while the absence of stress in the

TABLE 1. Acquisition of TWAT in Different Perinatal Influences

Group	Prenatal alcoholization	Postnatal stress	Acquisition of TWAT
1. Alcoholized stressed rats	+	+	Impaired
2. Alcoholized nonstressed rats	+	-	Unchanged
3. Nonalcoholized stressed	-	+	Improved
4. Nonalcoholized nonstressed	-	-	Unchanged

early postnatal period reduces the negative effects of prenatal exposure to ethanol.

We have obtained an apparently paradoxical result — the absence of impairment in learning TWAT in prenatally alcoholized rats without subsequent stress (group 2) in comparison with nonstressed controls (group 4). The impairment of learning in alcoholized offspring was observed only in the animals subjected to postnatal stress (group 1). This suggests that in some cases the disturbances in the high integration functions of CNS in the offspring from mothers receiving alcohol during pregnancy can be induced not by ethanol and its metabolites, but caused by some other factors. Being neutral or even positive in healthy animals, these factors become adverse in alcoholized animal due to higher sensitivity of their brain. Mild stress probably is one of such factors, which can modulate the level of hormones and catecholamine metabolism [5] in prenatally alcoholized offspring during the early ontogeny due to their hyperreactivity to stress [8]. This probably results in long-term changes in the regulatory mechanisms of the hypothalamo-pituitary-adrenocortical axis, modulates the activity of protein- and nucleic acid-synthesizing enzymes, and, consequently, affects the growth and differentiation of the nervous tissue [11].

An enhanced synthesis of informational molecules observed in information-enriched environment [1-3], in particular, after handling, and probably determining higher behavioral abilities in healthy animals, can be abolished by prenatal exposure to ethanol, which is known to disturb protein metabolism in the brain during the postnatal period [4].

Thus, our findings suggest that mild stress during early postnatal ontogeny, which enriches the environment and improves learning in healthy offspring in the adulthood, can become a pathogenic factor and impair the higher nervous activity in offspring subjected to prenatal alcoholization.

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