Dose-Dependent Effects of β-Phenylglutamic Acid Hydrochloride (RGPU-135, Neuroglutam) on Animal Behavior
I. N. Tyurenkov, V. V. Bagmetova, Yu. V. Chernyshova, and O. V. Merkushenkova

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β-Phenylglutamic acid hydrochloride (RGPU-135, neuroglutam) in doses of 13-650 mg/kg suppressed depressive behavior of animals in the Porsolt test (i.e. produced antidepressant properties), reduced anxiety in the open-field, elevated plus maze, and Vogel conflict tests (i.e. produced anxiolytic effects). RGPU-135 in doses of 26-130 mg/kg exhibited more pronounced antidepressant action and in doses of 26 and 52 mg/kg had more pronounced anxiolytic effects. RGPU-135 in doses of 13-78 mg/kg increased locomotor and exploratory activity of animals in the open-field test. Activating effects of this agent decreased with increasing the dose. RGPU-135 in the subtoxic dose (650 mg/kg) suppressed locomotor activity of animals (produced sedative effect).

Key Words: β-phenylglutamic acid hydrochloride; behavior; dose-effect; glutamic acid; psychotropic effect

β-Phenylglutamic acid hydrochloride (laboratory code RGPU-135, glutaron, neuroglutam) exhibited a wide spectrum of psychotropic effects: antidepressant, anxiolytic, neuroprotective actions in combination with nootropic, activation, and immunomodulatory properties [1,5-7]. This substance is characterized by low toxicity and potentially high safety [2,3] and therefore is a promising substance for clinical practice. At the stage of preclinical testing, possible relationships between the psychotropic effects of RGPU-135 and its dose should be studied.

Here we studied the dose dependence of the effects of β-phenylglutamic acid hydrochloride on animal behavior.

MATERIALS AND METHODS

The experiments were approved by the Regional Independent Ethic Committee of Volgograd Medical Research Center (protocol No. 140-2011, July 11, 2011) and conducted in accordance with GOST R 53434-2009 Principles of Appropriate Laboratory Practice and European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (1986). The experiments were performed on 56 outbred male rats weighing 180-220 g (8 rats per experimental point; Breeding Center Rappolovo, Russian Academy of Medical Sciences). The animals were kept under standard vivarium conditions with natural light-dark regimen, 20±2°C, 60% humidity, and free access to water and complete granulated feed (GOST R 50258-92).

The doses of RGPU-135 for the study of potential dose-dependent effects on animal behavior were chosen in accordance to the data on acute toxicity and our previous results [2,3,5]. Experimentally proved therapeutic dose of the agent 26 mg/kg constituting $\frac{1}{300}$ LD$_{50}$ [3,5] served as a basic dose and other doses used in our study were multiple of this dose: 13 mg/kg ($\frac{1}{600}$ LD$_{50}$), 52 mg/kg ($\frac{1}{150}$ LD$_{50}$), 78 mg/kg ($\frac{1}{100}$ LD$_{50}$), and 130 mg/kg ($\frac{1}{60}$ LD$_{50}$). The dose of 650 mg/kg (25-fold surpassing the therapeutic dose, $\frac{1}{10}$ LD$_{50}$) that can be considered as the subtoxic dose was also used in the experiment. Animal behavior was evaluated in psychopharmacological tests [4]: Porsolt...
forced swimming test, open-field test, elevated plus maze, and Vogel conflict test. RGPU-135 in study doses was administrated intragastrically in 2% starch mucilage 60 min before the beginning of experiments. Control animals received same volume of 2% starch mucilage.

Statistical analysis of obtained data was performed using Statistica 6.0 and BioStat 2008 software and rank univariate Kruskal–Wallis test and Newman–Keuls criterion.

RESULTS

RGPU-135 in doses of 26-130 mg/kg decreased the severity of depressive behavior in animals in the Porsolt forced swimming test. Under these conditions, the duration of immobility significantly decreased (Fig. 1, b), the latent period (LP) of immobility (Fig. 1, a), number of jumps (Fig. 1, c), and duration of active swimming (Fig. 1, d) increased. These data reflect antidepressant properties of RGPU-135. The most pronounced antidepressant effect was observed after administration of RGPU-135 in a dose of 26 mg/kg. Increasing the dose was followed by weakening of the antidepressant effect. RGPU-135 in a dose of 13 mg/kg did not affect LP of immobility, but significantly reduced its duration and increased the parameters of active avoidance (number of jumps, and duration of active swimming), which attests to primarily activating effect of this dose. The subtoxic dose of the agent (650 mg/kg) also produced a slight antidepressant effect, which was seen from significantly reduced duration of immobility; however, the decrease in the number of jumps observed in these animals can reflect its sedative effect. According to the results of Porsolt test, the antidepressant effect of neuroglutamin in the studied doses decreased in the following order: 26>52>78=130>13>650 mg/kg.

In the open-field test, RGPU-135 in doses 3>26>52>78 mg/kg produced activating effect and increased spontaneous motor (Fig. 2, a) and exploratory (Fig. 2, b) activities. The agent in a dose of 13 mg/kg had the most pronounced activating effect: motor activity of animals received this dose was significantly higher than after administration of other doses. Administra-