

Effect of Chronic Caffeine Consumption on Changes in Locomotor Activity of WAG/G and Fischer-344 Rats Induced by Nicotine, Ethanol, and Morphine

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We studied the effect of single treatment with nicotine, ethanol, and morphine on locomotor activity of WAG/G and Fischer-344 rats chronically drinking caffeine solution. In Fischer-344 rats receiving caffeine locomotor activity in the open-field test was much lower than in animals drinking water, while in WAG/G rats no differences in locomotor activity were found. Chronic caffeine intake increased rat sensitivity to the stimulating effect of nicotine and ethanol, but decreased their sensitivity to the depressant effect of morphine. Chronic caffeine treatment most significantly modulated the effects of nicotine, ethanol, and morphine in Fischer-344 rats.

Key Words: rats; locomotor activity; caffeine; nicotine; ethanol; morphine

Caffeine is widely consumed by humans. Coffee, tea, cacao, and cold drinks contain a considerable amount of this psychoactive substance. Civilized people consume caffeine in a daily dose of 3.0 mg/kg primarily with coffee [6]. Single administration of caffeine possessing psychopharmacological activity produces psychostimulant, anxiogenic, and other effects [7,9,12]. Chronic consumption of caffeine also has a psychotropic effect [4]. Acute and chronic administration of caffeine modulates the effects of other psychoactive substances, including amphetamine [10], cocaine [11], and morphine [8]. Caffeine increases positive reinforcement properties of alcohol and nicotine. The products containing these substances are often consumed together with each other (triple "c": coffee, cognac, and cigar). The influence of chronic caffeine consumption on the sensitivity to acute effects of psychoactive substances consumed by people is poorly studied.

Here we studied the effect of single treatment with nicotine, ethanol, and morphine on locomotor activity of rats chronically receiving caffeine with drinking water. Our previous studies showed that WAG/G and Fischer-344 rats differ in their sensitivity to acute and chronic effects of caffeine [2,4].

MATERIALS AND METHODS

Experiments were performed on male WAG ($n=64$) and Fischer-344 rats ($n=64$) weighing 180-200 g. Before the experiment the animals were housed in cages (8 rats per cage) and had free access to standard feed and drinking water. The light/dark period was 12:12 h (daytime 9.00-12.00).

The rats were divided into 2 groups (32 animals of each strain). Some rats received 0.1% caffeine solution instead of drinking water for 30 days. Other rats drank water in this period.

On day 30 the animals were placed in a square open field (50×50 cm). Locomotor activity was recorded automatically with infrared sensors fixed in walls of the open field. Control ($n=8$) and experimental animals ($n=8$) of each strain were injected with nicotine

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(1 mg/kg subcutaneously), ethyl alcohol (1.5 g/kg intraperitoneally), morphine hydrochloride (10 mg/kg intraperitoneally), or isotonic NaCl 30 min before the open-field test.

The results were analyzed by Student's *t* test and analysis of variance.

RESULTS

The mean daily fluid consumption in different groups was 25.0 ± 1.3 ml. No differences were revealed in water and caffeine consumption. The rats drinking 0.1% caffeine solution received caffeine in a daily dose of 100 mg/g. This corresponds to high consumption of caffeine by some people. In the open-field test locomotor activity of Fischer-344 rats receiving caffeine was lower than in animals drinking water. No differences were found in locomotor activity of WAG/G rats (Table 1).

Nicotine and ethanol increased locomotor activity of WAG/G and Fischer-344 rats (Figs. 1, 2). Chronic caffeine consumption slightly decreased the sensitivity to nicotine in WAG/G rats, but increased it in Fischer-344 rats (Fig. 1). Chronic caffeine consumption increased rat sensitivity to the activating effect of ethanol. These changes were most pronounced in Fischer-344 rats (Fig. 2).

Morphine prolonged the time of passive behavior and suppressed locomotor activity of WAG/G and Fischer-344 rats. The depressant effect of morphine was most pronounced in Fischer-344 rats. It should be emphasized that chronic caffeine consumption abolished the depressant effect of morphine in Fischer-344 rats (Fig. 3).

Our results suggest that chronic caffeine consumption increased the sensitivity to the stimulating action of psychoactive substances, but decreases their sensitivity to the depressant effects. Chronic caffeine consumption most significantly modulated the effects of nicotine, ethanol, and morphine in Fischer-344 rats. Published data show that single or chronic consumption of caffeine suppresses intravenous morphine self-administration behavior in WAG/G rats [4]. Our previous studies demonstrated that Fischer-344 rats differ from WAG/G rats in higher degree of anxiety [13]. The density of benzodiazepine receptors [1] and the content of anxiolytic peptides in various brain regions were low in these animals [3,5]. These peculiarities

TABLE 1. Locomotor Activity of Rats in the Open Field (arb. units)

Group	WAG/G	Fischer-344
Water	11.11 ± 2.40	12.75 ± 2.50
Caffeine	14.25 ± 3.10	6.44 ± 1.95

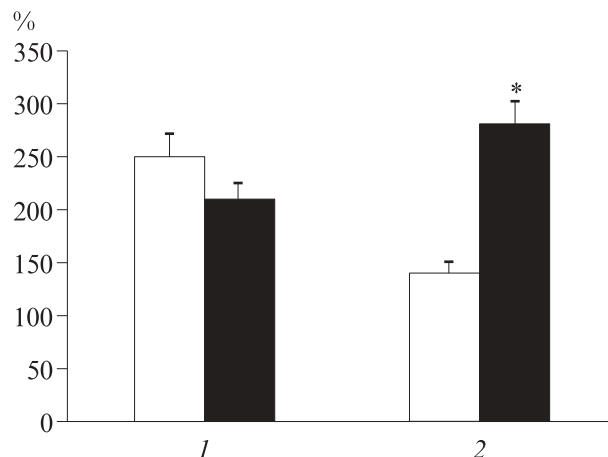


Fig. 1. Effect of caffeine on locomotor activity of WAG/G (1) and Fischer-344 rats (2) receiving water (light bars) or caffeine (dark bars). Ordinate: locomotor activity (%). Locomotor activity of rats not receiving nicotine was taken as 100%. Here and in Figs. 2 and 3: * $p < 0.01$ compared to animals consuming water.

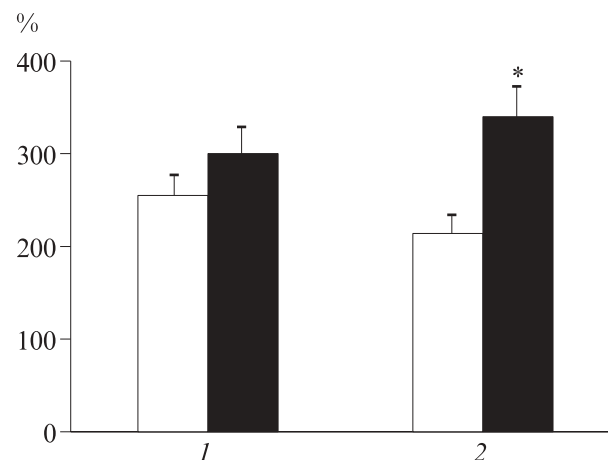


Fig. 2. Effect of ethanol on locomotor activity of WAG/G (1) and Fischer-344 rats (2) receiving water (light bars) or caffeine (dark bars). Ordinate: locomotor activity (%). Locomotor activity of rats not receiving ethanol was taken as 100%.

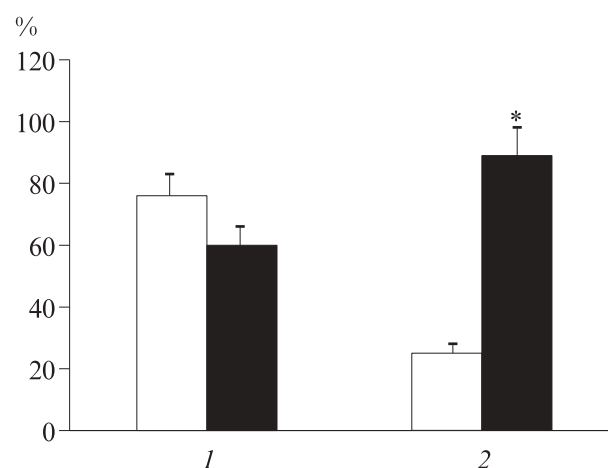


Fig. 3. Effect of morphine on locomotor activity of WAG/G (1) and Fischer-344 rats (2) receiving water (light bars) or caffeine (dark bars). Ordinate: locomotor activity (%). Locomotor activity of rats not receiving morphine was taken as 100%.

probably contribute to changes in the sensitivity to psychoactive substances after chronic caffeine consumption. The people having these genetically determined or acquired characteristics display different sensitivity to the chronic effect of caffeine.

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