

The trans-isomer of resveratrol acutely improves motivation in rat



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Introduction

Resveratrol (3,5,4'-trihydroxy-trans-stilbene), a natural non-flavonoid polyphenol antioxidant, exists as two geometric isomers: cis- and trans-. The trans-isomer of resveratrol is the active ingredient of *Poligonum cuspidatum*, and it is also found abundantly in the skin of red grapes and red wine. It has been shown that more stable trans-resveratrol demonstrates a variety of pharmacological activities including antioxidant, anti-inflammatory, neuroprotective properties and amelioration of learning and memory impairment (1), (2) and (3). However, its behavioral profile still remains controversial.

The goal of the present study was to examine the influence of trans-resveratrol and compare its dose-response effects on memory and depression-like behavior.

Materials and methods

Animals and drugs

Experiments were carried out on adult male Wistar rats. The substances were suspended in a solvent containing dimethyl sulfoxide - DMSO, and were administered intraperitoneally, in a volume of 1 ml/kg. The number of rats per treatment group was 7-8. We independently studied the effects of trans-resveratrol (5–20 mg/kg) on retention versus acquisition of active avoidance (AA) and depression-like behavior in the forced swim test (FST). We also tested the locomotion to exclude the excitatory or inhibitory effects.

Forced swim test (FST)

FST was performed in a glass cylinder, 45 cm high, 20 cm diameter filled with water up to a height of 30 cm, with a temperature of 21–23 °C. Male Wistar rats were exposed to two swimming sessions (an initial 15-min pretest session, followed 24 h later by a 5-min test session). The duration of immobility (seconds) was scored during the 5-min test session and the rat was considered immobile whenever it floated passively in the water and only made movements necessary to keep its head above the water line. The time of struggling (seconds) during the 5-min test session consists of explosive muscular movements against the apparatus wall, in an attempt to escape from the cylinder.

Conflict of interest statement

We declare that we have no conflict of interest

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Active avoidance test (AA)

AA test was performed in automated two-way shuttle boxes and programming recording units (Campden Instruments, Sileby, UK). In the first part of the study, the active avoidance task was elaborated by 100-trial 2-day sessions, and in the second part the influence of trans-resveratrol on the acquisition rate was checked in a procedure lasting five consecutive days, with 50 trials per day.

Measurement of locomotor activity

Twenty minutes after receiving the treatment or solvent, single rats were placed in a clear Plexiglas chamber (40 x 25 x 35 cm). Activity under dim red light (20 lux) was recorded for a total of 30 min, without any habituation period, using ANY-maze Video Tracking System software (Stoelting Co., Wood Dale, IL, USA)

Results

In FST, during the test session, the average immobility time of animals, in seconds, for the vehicle and resveratrol (5, 10, 20 mg/kg) was 145.3, 147.3, 94.7 and 66.0, respectively. ANOVA indicated statistically significant effects of resveratrol ($F(3,20)=50.95$, $p<0.001$). Dunnett's analysis showed that resveratrol significantly decreased immobility time at the doses of 10 and 20 mg/kg, exerted acute antidepressant-like effects (Fig. 1).

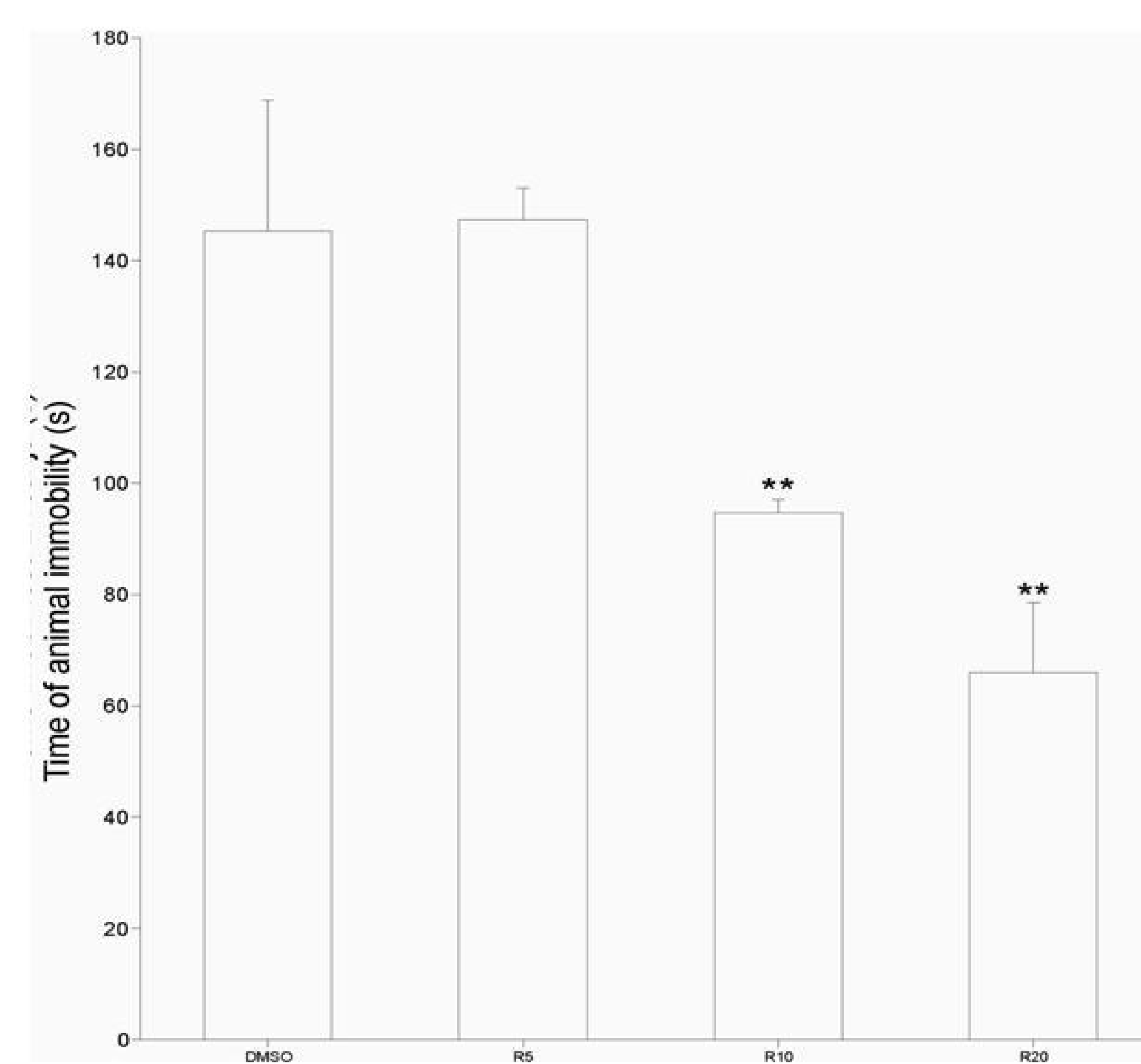


Fig 1. The effects of resveratrol (R: 5, 10, 20 mg/kg) on the immobility time of the animals in forced swim test; ** $p<0.001$ compared to solvent group (DMSO).

Treatment with trans-resveratrol significantly affected retrieval of avoidance responses on the second day of shuttle box testing. Dunnett's test indicated that the trans-resveratrol avoidance-facilitatory dose was 20 mg/kg (Fig. 2). However, it did not induce significant differences in acquisition rate during 5 days training.

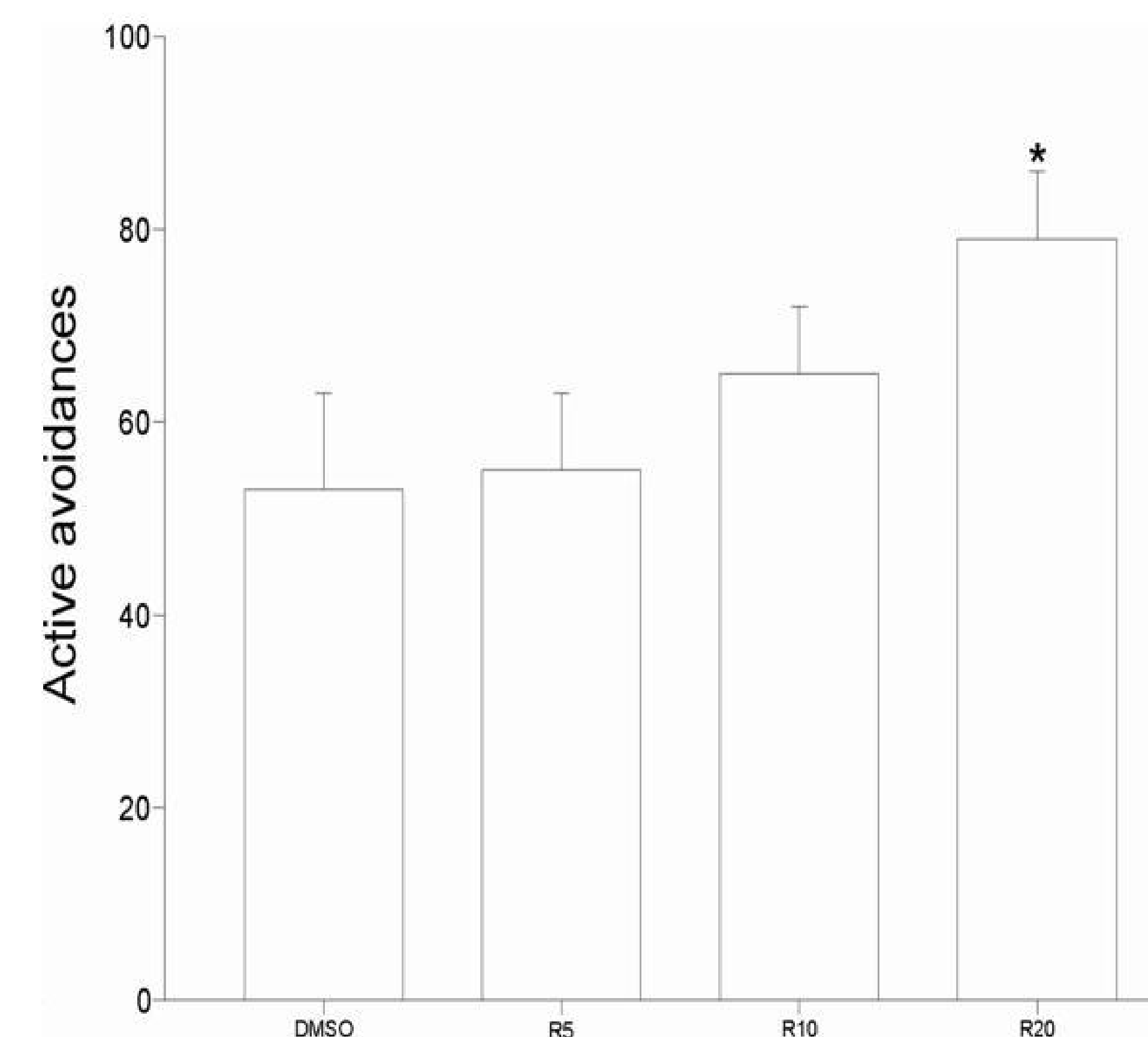


Fig 2. The effects of resveratrol (R: 5, 10, 20 mg/kg) on active avoidance retrieval; * $p<0.05$ compared to solvent group (DMSO).

ANOVA did not show a significant effect of treatment on the locomotion and rearing of the animals during 30 min of monitoring of spontaneous locomotor activity, $p>0.05$.

Table 1.

Table 1. Spontaneous locomotor activity in the open field test

Treatment	Locomotion	Rearing
DMSO	83 ± 7	13 ± 5
Resveratrol 5 mg/kg	84 ± 14	14 ± 5
Resveratrol 10 mg/kg	84 ± 2	16 ± 3
Resveratrol 20 mg/kg	92 ± 8	14 ± 3

Conclusions

⇒ Our results experimentally support the findings that under certain circumstances, trans-resveratrol, produces acute memory-enhancing and antidepressant-like effects

⇒ These behavioural effects were not confounded by locomotion influences

⇒ This study is going to be extended in the characterizing the repeated dose administration of resveratrol and clarifying the probable central mechanism of its action.

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