Differential behavioural effects of chronic oral administration of acetyl-L-carnitine in young and old rats

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DIFFERENTIAL BEHAVIOURAL EFFECTS OF CHRONIC ORAL ADMINISTRATION OF ACETYL-L-CARNITINE IN YOUNG AND OLD RATS

W.G.M. Raaijmakers, A. Blokland, F.J. van der Staay and J. Jolles

Department of Neuropsychology and Psychobiology, University of Limburg, P.O. Box 616, 6200 MD Maastricht

ABSTRACT

Young and old Wistar (Bor: WISW (SPFCpb)) rats were chronically treated with acetyl-L-carnitine (ALCAR). The treatment decreased activity in the open field of old but not young rats. In a spatial seven-choice discrimination procedure the treatment improved the performance of young rats on the learning of a second task ('reversal'); the untreated old rats were already superior to the untreated young rats and no effect of ALCAR was found on their performance. The effects of ALCAR and the age differences found are interpreted as reflecting differences in attentional processes.

INTRODUCTION

Acetyl-L-carnitine (ALCAR) is the acetylic derivate of carnitine. Both compounds play an important role in the energy and lipid metabolism of cells. Chronic ALCAR treatment has been reported to exert anti-ageing effects with respect to various neuroanatomical and neurochemical changes, particularly in the hippocampus (Badiali De Giorgi et al., 1987). Only few data are available on the behavioural effects of chronic ALCAR treatments (e.g. Ghirardi et al., 1988).

We studied open-field behaviour and spatial discrimination learning in young and old untreated and ALCAR-treated rats. We hypothesized that chronic ALCAR consumption would differentially influence the behaviour of the young and aged rats.

MATERIALS AND METHODS

Animals. Sixteen 2-month-old and sixteen 23-month-old male Wistar rats were matched for body weight and assigned to one of two treatments. All animals were housed individually in standard Makrolon cages and had free access to food and water. They were kept under a reversed light-dark cycle.

Treatment. Six weeks after the initial matching the ALCAR-treated groups

were given 50 mg/kg/day ALCAR, which was dissolved in a 0.1% saccharine solution. The control groups received a comparable amount of saccharine solution. Six weeks after the start of the treatment the rats were tested in the open-field. The treatment was continued during testing.

Open field test.

Apparatus and procedure. The floor of the open field (100x100x30 cm) was subdivided into 36 equal squares and dimly illuminated (ca 2 lux). The rats were put in the apparatus on four consecutive days and observed in five-minute sessions. The number of lines crossed were registered. The data from the four sessions were aggregated.

Seven-choice spatial discrimination task.

Apparatus. The 8-alley radial maze consisted of a central platform from which 8 alleys radiated equidistantly. A cylindrical door that opened by moving down vertically allowed simultaneous access to the eight alleys. Symbols above the entrances of the alleys provided distinct intra-maze cues.

Procedure. Thirteen weeks after the start of the treatment the rats were tested in the seven-choice spatial discrimination task. They had been tested before in another spatial discrimination task in the conefield. A differential food-deprivation was applied: the body weights of the young and old rats were reduced to 85% and 80% respectively of their free-feeding value to ensure comparable levels of motivation in both age groups.

The rats were trained with massed trials (5 trials per day) until a criterion of seven errorfree trials in a series of nine trials was reached. A trial was terminated as soon as the rat had found the food reward. Rats could enter and re-enter all alleys (including the start alley) freely during a trial. The day after a rat had reached criterion on this problem (task A), a second, similar problem (task B) was presented. In task B a different set of start and goal alleys was used. In task A, the goal alley was 135° to the right of the start alley, whereas it was 135° to the left of the start alley in task B. Trials to criterion and errors to criterion were analyzed.

RESULTS

Open field test. The activity of the rats, expressed as mean number of line crossings, is presented in Fig. 1. This activity measures provides a valid measure of anxiety in rats (Van der Staay et al., 1990). Since we do not know whether age differences in line crossings as found between the two control groups ($t_{14}=4.10$, $p<.01$) can be interpreted in the same way as differences between groups of the same age, the effect of ALCAR is evaluated

statistically within age groups. Chronic ALCAR-treatment decreased the activity of the old rats ($t_{14}=2.30$, $p<0.05$) but had no effect in the young rats (reported in more detail by Blokland et al., 1990).

Spatial discrimination. No differences between groups were found with respect to the acquisition of task A. The results for the acquisition of task B are presented in Fig. 2. ALCAR-treated rats needed less trials to reach the criterion ($F_{1,28}=5.23$, $p<0.05$); age differences were not found. A similar treatment effect was found for errors to criterion ($F_{1,28}=12.49$, $p<0.01$). The old rats made less errors during the acquisition of task B ($F_{1,28}=8.87$, $p<0.01$). The beneficial effect of the ALCAR treatment was stronger in the young than in the old rats (age by treatment interaction: $F_{1,28}=6.96$, $p<0.05$).

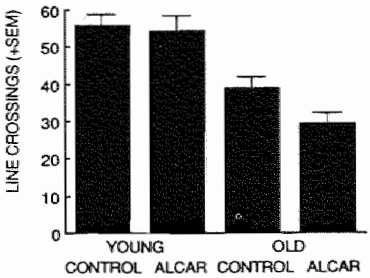

Fig. 1 Line crossings (+ SEM) in the open-field test of untreated and ALCAR-treated 5-month-old and 26-month-old Wistar rats.

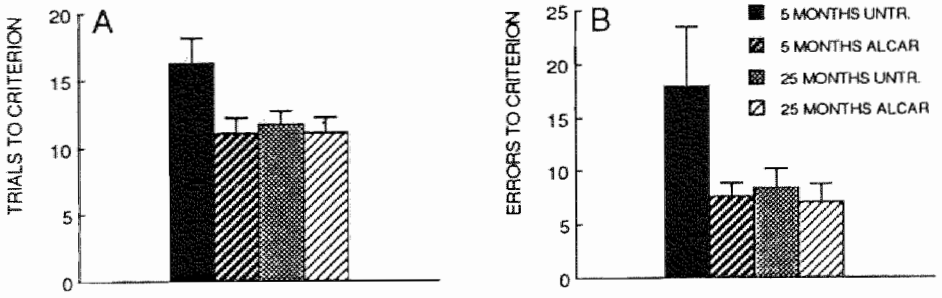

Fig. 2 Trials to criterion (A) and errors to criterion (B) in task B of the seven-choice spatial discrimination in an eight-alley radial maze.

DISCUSSION

The decreased activity in the open field of the old rats suggests an increase in emotional reactivity. The lack of data on the validity of this measure across ages, however, makes this interpretation premature. Chronic oral administration of ALCAR increased the emotional reactivity of the old rats but not of young rats. It can be speculated that this effect might be related to an increase in arousal if we assume that the old animals have a higher basal level of arousal than the young rats. Evidence for this notion is provided by the finding of higher basal levels of corticosterone in old male rats (Sapolsky et al., 1984).

The absence of an age difference in acquiring task A in the radial maze is in contrast to the finding of impaired performance in old animals by Raaijmakers et al. (see elsewhere in this volume). Since daily sessions of five instead of three trials were used, the animals could reach the criterion within two instead of three days. Goodrick (1973), for example, found that a procedure of massed trials facilitates spatial discrimination learning in aged rats. Comparison of the findings from the present experiment (data not shown) with those of Raaijmakers et al. (see elsewhere in this volume) indicates that the old animals have improved in performance because more training trials were given in succession.

With regard to task B, the better performance of the old animals as well as the facilitation of the performance of the young animals by ALCAR may be caused by different levels of arousal in the groups. Our procedure of learning task B after the criterion on task A has been reached, is comparable to reversal learning in other mazes. Reversal learning is facilitated by a heightened level of arousal (Landfield et al., 1981). The facilitation of the performance of the young animals might have been mediated by an ALCAR-induced increase in the level of arousal. Due to a presumed high basal level of arousal of the old animals, treatment with ALCAR might be ineffective to improve the performance in this age group. Other interpretations, however, cannot be excluded. Further research is needed to establish whether ALCAR influences behaviour by increasing attentional processes.

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