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Effects of Sodium Azide on Motor Activity, Motor Coordination, and Learning

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LALONDE, R., C. C. JOYAL AND S. BEAUDIN. *Effects of sodium azide on motor activity, motor coordination, and learning.* PHARMACOL BIOCHEM BEHAV **56**(1) 67–71, 1997.—Because of the proposed importance of cytochrome oxidase in some neurological disorders, an inhibitor of this enzyme was evaluated in a battery of tests measuring exploration, motor coordination, and learning. Mice injected with sodium azide (6 or 12 mg/kg) were slower to initiate a response in a T maze and had less rears in a small chamber than mice injected with placebo. Drugged mice did not alternate spontaneously even at a minimal retention interval (0 min), but were not impaired in water maze spatial and visual discrimination learning tasks. No group differences emerged in terms of horizontal motor activity and its habituation, number of grooming episodes, and motor coordination. These results indicate that azide-induced slowing of motor activity is situation-specific and is accompanied by abnormalities in choice behavior in a T maze. **Copyright © 1997 Elsevier Science Inc.**

Azide Motor activity Spatial learning Motor coordination

IT has been suggested that some neurological diseases affecting the brain and muscle are due to selective abnormalities of mitochondrial enzyme activity. Cytochrome oxidase deficiency in the brain may be associated with the neurological disorders found in Kearnes-Sayre syndrome (3), Leigh's syndrome (6), and Alzheimer's disease (15). Kearnes-Sayre syndrome is sometimes accompanied by a cerebellar disorder while severe cognitive deficits are associated with the other two syndromes. The question therefore arises as to whether cognitive or motor impairments may be due to cytochrome oxidase deficiency. One way to investigate this possibility is with the use of sodium azide (NaN_3), a drug which at low doses causes a selective impairment in cytochrome oxidase activity without affecting the activity of other mitochondrial enzymes (2). Bennett and Rose (1) found that sodium azide, administered subcutaneously via a minipump, causes spatial learning deficits in the Morris water maze without affecting horizontal motor activity and proposed that sodium azide may serve as an experimental model of Alzheimer's disease.

The purpose of the present study was to evaluate the effects of sodium azide in a wide range of behavioral tasks in order to determine the extent to which this drug affects cognitive as opposed to motor or motivational deficits. Based on preliminary experiments in CD-1 mice, behaviorally relevant doses were determined to be in the 0–12 mg/kg IP range, because a higher dose (25 mg/kg) resulted in some cases in death after one or two injections. The LD_{50} in CD-1 mice is approximately 0.5 mmol/kg (32.5 mg/kg) (17). Since death caused by azide was not reversed by oxygen, it is not caused by tissue hypoxia (16). Mortality in azide-injected CD-1 mice is often accompanied by convulsions and was decreased by phenobarbital, but not by diazepam, phenytoin, and ketamine/xylazine (17), implying mediation by an unknown central nervous receptor sensitive to barbiturates. A single dose of 14 mg/kg IV caused convulsions in 10/11 monkeys and death from respiratory arrest in 2/11. Ataxia occurred in 5/11 monkeys, with neuropathological evidence of cerebellar damage in 4/11 (13). Basal ganglia neuropathology and abnormal movements occurred in monkeys with chronic administration of sodium azide (12). In pentobarbital-anesthesized cats, seizures occcurred at 10 mg/kg IV (7). In the first experiment of the present study, no death occurred at 6 mg/kg, while 1/7 died at 12 mg/kg. Behavioral evaluations began 1 h postinjection. We were unable to find a study measuring brain content of azide at different postinjection intervals. In CD-1 mice, azide is still present in the blood at 1 h postinjection but is very low at 2 h postinjection (17). At no time did the animals completing the experiment appear sick or lose weight.

MATERIALS AND METHODS

Animals

In the first experiment, 26 naive CD-1 male mice (1–2 mo of age) were obtained from Charles-River Canada (St-

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Constant, Quebec), placed in group cages of 8–10 in a temperature controlled room and evaluated in a separate experimental room. Food and water were available at all times. A separate shipment of CD-1 mice was used for Experiment 2 (habituation). A third shipment was used for Experiment 3 (discrimination learning), but this time with B_6C_3/a-a mice, because CD-1 mice, being albino, have great difficulty in learning this task and so the use of non-albino mice was appropriate.

Apparatus

A T maze (stem: 82 × 8.5 cm; arms: 30 × 8.5 cm; height of walls: 10.2 cm) made of transparent plastic was used, together with an inclined (45 degrees) screen made of wire mesh (35 × 35 cm, 12 squares/10 cm) surrounded by a wooden frame. Horizontal motor activity was measured in one half of the stem portion of the T maze (41 × 8.5 cm), separated into four equally spaced squares by means of adhesive tape under the maze. Vertical motor activity was measured in an enclosed plastic chamber (19 × 25 cm, height of walls: 16 cm). Motor coordination was measured with a coat-hanger of triangular shape made of steel (horizontal bar: 40 cm, side-bars: 19 cm, 45 degree angle, bar width: 2 mm). The plastic water maze was rectangular (45 × 35 cm, height of walls: 13 cm, water level: 10 cm) with a grid-covered platform (overturned beaker, diameter: 6.5 cm) found at various locations. The same apparatus was used for water maze discrimination learning. Habituation to motor activity was measured in an enclosed field (27 × 30 cm) containing six squares delineated by means of adhesive tape. The box was made of grey opaque plastic and the height of the walls was 13.4 cm.

Procedure

In Experiment 1, the following tests were used: spontaneous alternation (days 1–13), inclined screen (days 1–3), horizontal motor activity (days 4–6), coat-hanger (days 7–9), vertical activity, grooming episodes (days 10–12), and water-maze learning (days 14–20). A week intervened between behavioral testing days 13 and 14. Body weight was measured on days 1, 13, 14, and 20. Twenty-one animals were randomly divided into three groups ($n = 7$) and injected IP with placebo (0.9% saline) or sodium azide (ICN Canada) at 6 or 12 mg/kg. One of the animals in the 12 mg/kg azide group died after 12 injections and was not replaced by another mouse until water maze testing on day 14. The results of the dead animal were not included in data collection.

In spontaneous alternation testing (4), the mice were placed in a shortened segment (41 × 8.5 cm) of the T maze and were forced to turn either to the right (on odd days) or to the left (on even days) arm, the opposite arm being blocked by a plastic barrier, and allowed to remain in that arm for 10 s. On days 1, 4, 7, 10, and 13, the mice were immediately placed back in the stem for trial two and allowed to choose either arm, the barrier being removed. On days 2, 5, 8, and 11, the mice were evaluated in other tests (see below) or kept in a holding cage for a 3 min duration (retention interval). On days 3, 6, 9, and 12, the same procedure was followed but with a retention interval of 10 min. Thus, three retention intervals were used: 0 (excluding the 10 s spent in the maze arm), 3 and 10 min. In all cases, between trial one and trial two, the maze was washed with water and dried with a paper towel in order to minimize odor cues. Trial two latencies were determined with a cut-off point of 60 s, after which time the mice were gently prodded forward until they made a choice. The latencies were defined as the amount of time elapsed between placement in the maze and choice of an arm (four paw criterion).

The inclined screen test of motor coordination consisted of three measures: latencies before a) the whole body faced upward after the mice had been placed in the downward direction, b) reaching the top of the screen (snout criterion) and c) a fall off of the screen occurred (cut-off point 60 s). There was one trial per day, conducted after alternation testing on day 1 and between trials one and two of alternation testing on days 2 and 3. Horizontal motor activity was tabulated in 4 min sessions, after alternation testing on days 4 and 5 and between trials one and two of alternation testing on day 6. The number of segments traversed (four paw criterion) in half of the stem portion (41 × 8.5 cm) of the T maze divided into four equally spaced segments was the activity measure. In the coat-hanger test of motor coordination (8), the mice were placed in the middle part of the horizontal bar facing the right side. Four latencies were determined (cut-off point: 60 s). Latency one is the amount of time elapsed between the start of testing and the placement of the two front paws on either side-bar of the coat-hanger. Latencies two and three are the amount of time elapsed between the start of testing and placement of three or all four paws respectively on the side-bar. Latency four is the amount of time elapsed before a fall. Successful climbs to the half-way point of the side-bar or up to the top were tabulated. There were two trials per day, separated by an intertrial interval of 3–4 min, the test being conducted after alternation testing on days 8 and 9 and between trials one and two of alternation testing on day 9. Vertical motor activity (number of rears: front paws raised in the air or against a wall) and the number of grooming episodes (defined by licking of any body part) were assessed in the enclosed chamber for 4 min, conducted after alternation testing on days 10 and 11 and between trials 1 and 2 of alternation testing on day 12.

In water-maze testing, an adaptation of the Morris maze (11) in that the enclosure was rectangular instead of circular, place learning (invisible platform condition) was evaluated on days 14–19 and visuomotor coordination (visible platform condition) on day 20, each with eight trials per day (intertrial interval: 5–10 min) and a cut-off point of 60 s. On trial one, the mice were placed against the wall of the basin in the middle part of the northern wall. On subsequent trials, the animals were placed in east, south, and west positions and rotated a second time in that order. Five additional mice were added to the 12 mg/kg azide group (now n = 11) for this test. There were two measures: the number of quadrants traversed (the pool being divided into four equally spaced quadrants by means of masking tape) and latencies before reaching the platform. The platform was located beneath water level (milky solution) in the north-west position on days 14–16 and in the south-east position on days 17–19 and above the water level (clear water) in the south-west position on day 20. Water was gently stirred between trials in order to minimize odor cues.

In Experiment 2, a separate group of 30 male CD-1 mice was randomly allocated into three groups: 0, 6, and 12 mg/kg. Since this experiment lasted only 3 days, there was a preinjection period of 12 days. Mice were injected with azide or placebo for 12 consecutive days and then placed in an enclosed field for 3 min on day 13. On that day, the mice were injected 60 min before the test. The number of segments traversed was measured. On the following day, the mice were injected once more and retested in the same apparatus. One week

TABLE 1

PERCENTAGE OF SPONTANEOUS ALTERNATION AND MEAN (SD) TRIAL TWO LATENCIES OF MICE INJECTED WITH SODIUM AZIDE OR PLACEBO

Group	Alternation Rate Retention Interval (Min)			Trial 2 Latencies (s)
	0	3	10	
Placebo	74**	71*	61	16.2 (4.1)
Azide 6 mg/kg	63	86**	57	31.9 (15)$^{+}$
Azide 12 mg/kg	57	63	54	27.9 (7.7)$^{++}$

* $p < 0.05$ vs chance levels; ** $p < 0.01$ vs chance levels; $^{+}$ $p < 0.05$ vs placebo; $^{++}$ $p < 0.01$ vs placebo.

later, the same procedure was used. Both intra- and inter-session habituation was measured.

In Experiment 3, a group of B_6C_3/a-a mice of either sex was used for water maze discrimination learning (10). The test was performed in the same basin as in spatial learning, except that two invisible platforms were placed below water level. The discriminanda were made of cardboard (height = 27.3 cm, width = 8.4 cm) held in place by masking tape behind and over the platforms against a white wall and touching water level. The positive stimulus (S+) was a white card with black horizontal stripes, and the negative stimulus (S-) was a black card. Because the background wall and basin were white, the appropriate S+ is the striped white card, because the use of the black card as the S+ would have made the task too easy. The positions of S+ and S- were determined by Fellows sequence one and three (5). The test was run until the mice reached criterion as defined by 13/16 correct responses (81%). Data was reported as number of trials to criterion excluding the criterion run. Whenever an error occurred, the S-platform was tipped over by the experimenter's hand in order to prevent the mice from climbing aboard. The platform associated with the S+ was enclosed in wire-mesh to facilitate climbing. There were eight trials per day, with the drug being injected 60 min before testing as in the two previous studies at 0 (n = 6), 6 (n = 7) and 12 (n = 9) mg/kg.

Data analyses

For group comparisons, parametric data were analyzed by means of ANOVA and non-parametric data by means of the Kruskal-Wallis test. For multiple comparisons, the t-test using the within-group variance was used for parametric data and the Wilcoxon rank sum test was used for non-parametric data. The spontaneous alternation results of each group were evaluated by the Mann-Whitney test in comparison to a theoretical control group performing at the 50% rate.

TABLE 2

MEAN (SD) VALUES OF INCLINED SCREEN TEST IN MICE INJECTED WITH SODIUM AZIDE OR PLACEBO

Group	Inclined Screen Latencies (s)		
	Till Turning	Till Reaching Top	Till Falling
Placebo	5.7 (3.1)	12.5 (5.1)	60 (0)
Azide 6 mg/kg	6.8 (2.3)	21 (13.1)	60 (0)
Azide 12 mg/kg	4.5 (3.4)	8 (4.4)	60 (0)

RESULTS

A 2 × 2 ANOVA with a repeated measure on the second factor revealed no group differences or interactions in terms of body weight either during the 1–13 day period or the 14–20 day period (data not shown). All animals completing behavioral testing appeared healthy and active. There was a significant weight increase on days 1–13, $F(1, 17) = 157.5, p < 0.001$, but not on days 14–20, $F(1,17) = 0.65, p > 0.1$.

The placebo group alternated above chance at the 0, U(7, 7) = 7 , $p < 0.05$, and 3, U(7,7) = 10.5, $p < 0.05$, but not at the 10-min retention interval, $p > 0.05$ (Table 1). The 6 mg/kg azide group only alternated at the 3-min retention interval, U (7,7) = 3.5, $p < 0.001$, while the 12 mg/kg azide group did not alternate at any interval, $p > 0.05$. The drugged groups had higher trial two latencies than the placebo group, $H(2) = 7.96, p < 0.05$; 6 mg/kg: $R(7,7) = 36, p < 0.05$; 12 mg/kg: R(6,7) = 23, $p < 0.01$. There were no significant correlations between alternation rates and trial two latencies (placebo: rho = −0.262; 6 mg/kg azide: rho = +0.094; 12 mg/kg azide: rho = −0.319; all three groups: rho = −0.328, $p > 0.05$).

There were no significant group differences in the inclined screen test, horizontal motor activity, the coat-hanger test, and the number of grooming episodes (Tables 2, 3, and 4). However, vertical motor activity was lower for the drugged groups in comparison to the placebo group, $F(2,17) = 3.89$, $p < 0.05$; $t(17) = 2.0$, $p < 0.05$ for 6 mg/kg and $t(17) = 2.63$, $p < 0.01$ for 12 mg/kg. Two 3 × 6 ANOVAs with repeated measures on the second factor (3 groups and 6 blocks of 4 trials) for days 14–16 and 17–19 revealed no significant group difference or interaction ($p > 0.05$) for the quadrant measure (Table 5) or the latency measure (data not shown) in spatial learning. A 3 × 2 ANOVA with a repeated measure on the second factor revealed no significant group difference or inter-

TABLE 3

MEAN (SD) LATENCIES SUCCESSFUL CLIMBS DURING COAT-HANGER TEST OF MICE INJECTED WITH SODIUM AZIDE OR PLACEBO

Group	Latency (s)				Climbs	
	1	2	3	4	Half-Way	To The Top
Placebo	30.8 (13.8)	36.1 (11.1)	36.7 (11.5)	(5.9)	0.3 (0.3)	0.3 (0.2)
Azide 6 mg/kg	46.6 (13)	47.7 (13.2)	48.8 (12)	53.0 (6.8)	0.2 (0.2)	0.2 (0.2)
Azide 12 mg/kg	32.5 (12.3)	35.8 (14.6)	37.3 (14.1)	55.2 (4.2)	0.5 (0.3)	0.5 (0.3)

TABLE 4

MEAN (SD) MOTOR ACTIVITY LEVELS AND GROOMING IN MICE INJECTED WITH SODIUM AZIDE OR PLACEBO

Group	Motor Activity		Grooming Episodes
	Horizontal	Vertical	
Placebo	14.6 (5.5)	6.6 (2.6)	0.8 (0.7)
Azide 6 mg/kg	15.6 (9.3)	4.4 (2.1)*	0.6 (0.3)
Azide 12 mg/kg	9.4 (3.5)	3.6 (0.7)**	0.6 (0.7)

* $p < 0.05$ vs placebo; ** $p < 0.01$ vs placebo.

action for the quadrant measure (Table 5) or the latency measure (data not shown) in the visuomotor coordination task.

In Experiment 2, there was no significant difference between any of the groups in terms of motor activity on any of the test days (Table 6). Intra-session habituation occurred in all three groups (p *t*-test). The drug did not increase motor activity on test days 2 and 3 (Table 6). Four of the 10 mice in the 12 mg/kg azide group died before completion of the study, but none of the animals in the other two groups died. There was no difference in acquisition of water maze discrimination learning as determined by the number of trials (means and SD) to criterion: placebo = 87 (49.7), azide 6 mg/kg = 94.4 (43.9), azide 12 mg/kg = 118.4 (17.5).

DISCUSSION

Bennett and Rose (1) found that sodium azide caused spatial learning deficits in the Morris water maze, but no decreases in horizontal motor activity. In the present study, no decrease in horizontal motor activity was observed in mice injected IP with sodium azide (Tables 4 and 6). However, sodium azide slowed down motor activity in other tests, such as vertical motor activity (Table 4) and trial two latencies in spontaneous alternation testing (Table 1). The drug did not result in motor coordination deficits as evaluated by the inclined screen and coat-hanger tests. Thus, azide-induced slowing was situation-specific. Mice injected with azide were slower to initiate a choice between maze arms, but, given time, were not less active, as assessed by segment crossings in the stem of the maze.

The placebo group alternated above chance at the 0 and 3 but not at the 10-min retention interval (Table 1). The lack of alternation behavior in the control group does not necessarily mean that these mice are unable to retain spatial information over that interval. Mice from other strains (C57 and B6) are able to (7, 9) and the CD-1 mice may reach a significant alternation rate with additional trials. However, use of the longest retention interval reduces the alternation rate to non-significant levels. The lack of alternation in the 12 mg/kg azide group cannot be ascribed to a memory deficit, because this lack was noted even at the shortest (0 min) retention interval. Instead, this result may be ascribed to disinhibitory tendencies (impulsive behavior) or a decrease in exploratory motivation. A decrease in exploratory motivation may also be a possible explanation for the decrease in vertical activity found in this group. However, this is not a generalized deficit, since this group was not less active in terms of horizontal activity. Moreover, no significant correlation was found in this group, or any other, between alternation rates and trial two latencies, an indication that the reduced alternation rate observed in this group is independent of motor slowing. The 6 mg/kg azide group alternated at the 3 but not at the 0 and 10 retention intervals. Although this result may seem paradoxical, such a pattern has been found before. Stevens and Cowey (13) reported that ventral hippocampal lesions in rats caused a lack in spontaneous alternation at a short (50 s) but not at a long (50 min) retention interval, a result that may be due to disinhibitory tendencies alleviated with the use of a longer retention interval. In the present study, there is no evidence that sodium azide causes a selective loss in spatial memory or even non-spatial memory (as determined by discrimination learning rates), although this does not exclude the possibility of a hippocampally mediated effect on behavior.

On the basis of azide-induced learning deficits in the Morris water maze, Bennett and Rose (1) proposed that the drug impaired hippocampally mediated behavior. In the present study, sodium azide altered behavior without affecting spatial learning in a similar water maze. Thus, sodium azide appears to cause a wider range of behavioral effects than losses in memory. The lack of effect in spatial learning may be due to the lack of constant exposure to the drug by means of the minipump technique employed by these authors. Perhaps constant exposure to the drug is a prerequisite for the learning defect to occur. Other methodological differences include the use of rats, a different dose (1 mg/kg/hr), infusion rates beginning from 7 to 21 days prior to behavioral testing, and the use of 4 trials per day instead of 8. We repeated the spatial learning experiment with four instead of eight trials per day and obtained the same negative result. Thus, it is still uncertain whether this treatment can serve as a model of the mental deficiencies seen in Alzheimer's or other neurological diseases

TABLE 5

MEAN (SD) NUMBER OF QUADRANTS TRAVERSED IN MICE INJECTED WITH SODIUM AZIDE OR PLACEBO IN WATER MAZE LEARNING WITH INVISIBLE PLATFORM IN NORTH-WEST QUADRANT ON DAYS 1–3 AND IN SOUTH-EAST QUADRANT ON DAYS 4–6 AND WITH VISIBLE PLATFORM IN SOUTH-WEST QUADRANT ON DAY 7

GROUP	Days						
	1	2	3	4	5	6	7
Placebo	49.7 (9.9)	43.6 (12.1)	35.7 (10.9)	35 (8.9)	39 (9.2)	28 (7.2)	21.6 (6.4)
Azide 6 mg/kg	56.9 (16.7)	55 (12.6)	32.7 (10.9)	45 (14.4)	36.1 (12.5)	33.9 (8.4)	24 (6.8)
Azide 12 mg/kg	68 (17.8)	44.2 (16.1)	41.3 (17.7)	45.4 (16.1)	33 (11.4)	31.2 (9.2)	22.7 (7.2)

TABLE 6

MEAN (SD) NUMBER OF SEGMENT CROSSINGS IN AN ENCLOSED BOX FOR MICE INJECTED WITH AZIDE OR PLACEBO DURING THE FIRST 90 S OR THE LAST 90 S OF TESTING (INTRA-SESSION HABITUATION) OR OVER 3 DAYS

Groups	First 90s	Last 90s	Day 1	Day 2	Day 3
Azide	52.2	22.5	36.8	19.3	18.6
0 mg/kg	(17.2)	(8.4)	(12.0)	(10.4)	(6.3)
Azide	49.8	21.0	35.5	18.3	17.0
6 mg/kg	(21.1)	(11.4)	(15.9)	(10.5)	(9.7)
Azide	34.8	14.0	22.5	11.8	14.5
12 mg/kg	(18.6)	(4.8)	(13.1)	(7.6)	(8.0)

associated with cytochrome oxidase deficiency. This may be resolved with additional cytochrome oxydase inhibitors and with the use of intracerebral injections of sodium azide. The results of our study indicate that other behavioral abnormalities may occur in addition to water maze deficits after chronic exposure with the minipump technique and that these may provide added usefulness of this method as an experimental model of cytochrome oxidase deficient conditions.

REFERENCES

1. Bennett, M. C.; Rose, G. M. Chronic sodium azide treatment impairs learning of the Morris water maze task. Behav. Neur. Biol. 58:72–75; 1992.
2. Bennett, M. C.; Diamond, D. M.; Stryker, S. L.; Parks, J. K.; Parker, W. D. Cytochrome oxidase inhibition: a novel animal model of Alzheimer's disease. J. Ger. Psychiat. Neurol. 5:93–101; 1992.
3. Bresolin, N.; Moggio, M.; Bet, L.; Gallanti, A.; Prelle, A.; Nobile-Orazio, E.; Adobbati, L.; Ferrante, C.; Pellegrini, G.; Scarlato, G. Progressive cytochrome c oxidase deficiency in a case of Kearns-Sayre syndrome: morphological, immunological, and biochemical studies in muscle biopsies and autopsy tissues. Ann. Neurol. 21:564–572; 1987.
4. Douglas, R. J. Cues for spontaneous alternation. J. Comp. Physiol. Psychol. 62:171–183; 1966.
5. Fellows, B. J. Chance stimulus sequences for discrimination tasks. Psychol. Bull. 67:87–92; 1967.
6. Hayasaka, K.; Brown, G. K.; Danks, D. M.; Droste, M.; Kadenbach, B. Cytochrome c oxidase deficiency in subacute necrotizing encephalopathy (Leigh syndrome). J. Inher. Dis. 12:247–252; 1989.
7. Kaplita, P. V.; Borison, H. L.; McCarthy, L. E.; Smith, R. P. Perpiheral and central actions of sodium azide on circulatory and respiratory homeostatis in anesthesized cats. J. Pharmacol. Exp. Ther. 231:189–196; 1084.
8. Lalonde, R. Exploration and spatial learning in staggerer mutant mice. J. Neurogenet. 4:285–292; 1987.
9. Lalonde, R.; Botez, M. I.; Joyal, C. C.; Caumartin, M. Motor abnormalities in lurcher mutant mice. Physiol. Behav. 51:523–525: 1992.
10. Lalonde, R.; Joyal, C. C.; Ct, C.; Botez, M. I. Delayed spontaneous alternation in lurcher mutant mice. Psychobiology 21:139–141; 1993.
11. Lalonde, R.; Joyal, C. C.; Ct, C.; Botez, M. I. Simultaneous visual discrimination learning in lurcher mutant mice. Brain Res. 618: 19–22; 1993.
12. Mettler, F. A. Choreoathetosis and striopallidonigral necroses due to sodium azide. Exp. Neurol. 34:291–308; 1972.
13. Mettler, F. A.; Sax, D. S. Cerebellar cortical degeneration due to acute azide poisoning. Brain 95:505–516; 1972.
14. Morris, R. G. M.; Garrud, P.; Rawlins, J. N. P.; O'Keefe, J. Place navigation impaired in rats with hippocampal lesions. Nature 297:681–683; 1982.
15. Parker, W. D.; Filley, C. M.; Parks, J. K. Cytochrome oxidase deficiency in Alzheimer's disease. Neurology 40:1302–1303; 1990.
16. Smith, R. P.; Gosselin, R. E.; Krsuzyna, R. Sodium azide poisoning. Ann Int. Med. 83:739; 1975.
17. Smith, R. P.; Louis, C. A.; Krsuzyna, R.; Krsuszyna, H. Acute neurotoxicity of sodium azide and nitric oxide. Fund. Appl. Toxicol. 17:120–127; 1991.
18. Stevens, R.; Cowey, A. Effects of dorsal and ventral hippocampal lesions on spontaneous alternation, learned alternation and probability learning in rats. Brain Res. 52:203–224; 1973.