Measuring attention in a Parkinson's disease rat model using the 5-arm maze test

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HIGHLIGHTS

• MPTP-induced Parkinson's disease (PD) rat model is widely used for studying PD.
• This animal model exhibits pathophysiological and behavioral similarities to PD.
• Using the 5-arm maze test, results revealed that PD rats show normal external attention.

ABSTRACT

Twenty to thirty percent of patients with Parkinson's disease (PD) suffer from not only motor disorder, but also symptoms of dementia, named Parkinson's disease dementia (PDD). Cognitive deficits in PDD include memory, recognition, and attention. Although patients with PDD show fluctuation of internal attention when taking an attentional test, they perform better when provided with an external cue, indicating that they have normal external attention. We examined visuospatial attention in a 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced PD animal model using the 5-arm maze test. After an 8-day training period, followed by a 2-day pre-lesion test in the 5-arm maze, male Wistar rats received a microinfusion of MPTP into the substantia nigra pars compacta, while controls underwent a sham operation procedure. Nine days after MPTP lesioning, the rats underwent an open field test, followed by a 2-day post-lesion test in the maze. The results showed that: (1) no motor impairment was observed 9 days after MPTP lesioning; and (2) in the post-lesion 5-arm maze test, cue illumination lasting 0.5 s resulted in a decrease in the percentage of correct responses compared to a 2 second cue in both the sham-operated and MPTP-lesioned groups and no difference was observed between these two groups. As far as we are aware, this is the first study examining visuospatial attention in the PD rat model using the 5-arm maze test. These results suggest that, as in patients with PDD, MPTP-induced PD rats show normal external attention function.

1. Introduction

Parkinson's disease (PD), a high prevalence neurodegenerative disorder in the elderly population, results in progressive motor dysfunction [1–3]. At 5 years after diagnosis of PD, 20–30% of patients suffer from not only motor impairment, but also cognitive deficits, including memory, recognition, and emotion deficits, a condition referred to as Parkinson's disease dementia (PDD) [4,5]. In particular, some patients with PD show impaired performance in an attentional task [6], mental rotation test [7], visuospatial test [8], and object working memory test [9]. In addition to the abovementioned impairments, attention deficit may also be associated with a visuospatial deficit [10], and some PD patients get lost in places with which they were previously familiar [11]. Attention, like a mental spotlight, is the first stage of cognition and determines what information will be processed. With an attentional deficit, a person cannot concentrate on processing information,
resulting in disruption of working memory, which, however, can also be caused by other mechanisms. Thus, it is worth examining whether attentional dysfunction is seen in the PD rat model.

PD is characterized by degeneration of dopaminergic (DA) neurons in the substantia nigra (SNc), leading to reduced dopamine release from terminals in the striatum. In a rat model, microinjection of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), a toxin selective for the DA system, into the SNc causes damage to the nigrostriatal DA system and produces a similar pathophysiology and behavior to those seen in PD. In terms of neurochemistry, behavior, and histopathology, the MPTP-induced PD rat model manifests the symptoms of PDD, for example, impairment of object recognition and working memory [12–15] and therefore is the most widely-used simple model of PD [12–16]. A complete analysis of the behavioral profile might provide further support for the validity of this model.

The 5-arm maze has been used to measure sustained visuospatial attention [17]. The objective of the present study was to use the 5-arm maze test to examine attentional function in MPTP-induced PD rats. The results showed that, as in patients with PDD, external attention in the MPTP-induced PD rat model is not impaired.

2. Materials and methods

2.1. Experimental subjects

Twelve-week-old adult male Wistar rats (466.8 ± 5.8 g; n = 45; National Laboratory Animal Center, ROC) were randomly assigned to groups of 4–5 and housed in acrylic cages (35 × 56 × 19 cm) in a temperature-controlled animal room (21 ± 1 °C) on a 12 h light-dark cycle (lights on at 07:00) with ad libitum access to food and water. Three days before the beginning of the 5-arm maze test and throughout the testing period, the rats were partially food-deprived for 23 h a day, with 1 h free access to food after the daily behavioral observations. All experiments were performed during the light phase of the day between 08:00 and 18:00. The experimental subjects were transferred from the animal room to a preparation room with dim illumination (red light of 28 lx). The behavioral tests were performed in a room adjacent to the preparation room containing the 5-arm maze with dim red illumination of 3 lx at the center of the maze. Except when being tested in the maze, the animal remained in the preparation room throughout each daily session. The experiments were performed according to the NIH Guide for the Care and Use of Laboratory Animals and were approved by the Animal Care Committee of Chung Shan Medical University (IACUC approval No: 738), all efforts being made to minimize animal suffering and reduce the number of animals used.

2.2. General procedures

Starting 2 days after their arrival, the rats were handled in the preparation room for 5 min per day on 3 consecutive days to reduce the level of anxiety and stress response caused by the experimenter and experimental environment. One day before the training session, the rat was placed in the 5-arm maze for habituation and to familiarize itself with the experimental context. The 8-day training session was divided into two 4-day periods, training session 1 (days 1–4) and training session 2 (days 5–8). After the 8-day training session, a 2-day pre-lesion test was performed in the 5-arm maze, then, on the next day, the rats underwent stereotaxic surgery and microinjection of MPTP into the SNc or sham operation with no MPTP injection. Nine days after MPTP lesioning, an open field test was performed, then, starting the next day, a 2-day post-lesion test was performed in the 5-arm maze. The maze was cleaned after each trial in order to avoid any possible use of olfactory cues. During testing, the experimenter was seated quietly at a distance of 0.5 m behind the start box and thus not visible to the experimental subjects. From this position, the experimenter manually operated the opening and closing of the doors and manually recorded the latency using a silent stopwatch by direct visual observation.

2.2.1. Design of the 5-arm maze

The 5-arm maze is shown in Fig. 1. The maze, made of opaque black PVC, was constructed based on the design reported by Durkin et al. [17], and comprised a small rectangular start box with a transparent, vertically sliding door connecting to a central circular platform (32 cm diameter). On the opposite side to the start box, five symmetrically-arranged adjacent arms in a trapezoidal shape (floor 29 cm at one end decreasing to 11 cm at the other end; length, 45 cm; height, 20.5 cm) radiated from the central platform at an angle of 120°. Access to the arms was enabled by apertures (8 × 8 cm) cut into the perimeter wall of the central platform which could be closed individually by vertically sliding doors made of opaque black PVC. The five arms were positioned symmetrically in the visual field of the rat in the start box. Each arm was equipped, at its far end, with a small circular cup in which a food pellet reward could be placed such that it was not visible to the subject until it had fully entered the arm. Each arm was covered with a roof with a LED light bulb at its center connected to a control box, which controlled which arm was illuminated and for how long. The light bulbs were not directly visible to the rat in the start box and reflection from all surfaces was reduced as much as possible.

2.2.2. Open field test

Nine days after MPTP lesioning, the rats underwent a 10 min motor function test in an open field consisting of a square arena (40 cm × 40 cm × 40 cm) as described in our previous report [14]. The following measurements were recorded: (1) total distance traveled in cm; (2) number of movements; (3) movement time; (4) rest time; and (5) center time, the time for which the center of the animal’s body was in the center of the open field (20 cm × 20 cm). The rat was placed in the center of the open field and its movement was recorded with an infrared recorder.

2.3. Surgery

The test rats received a bilateral microinjection of MPTP-HCl (Sigma Chemical Co., St. Louis, MO, USA; 1 μmol in 2.1 μl of saline) into the SNc. Control rats underwent sham operation performed in the same way with bilateral microinjection of 2.1 μl of saline. The rats were anesthetized using Zoletil 50 (20 mg/kg, IP; Virbac, Carros, France), then MPTP or saline was bilaterally infused through a 30-gauge stainless steel needle using the following coordinates adapted from the rat brain atlas [18]: anteroposterior (AP), −5.0 mm from the bregma;

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**Fig. 1.** The 5-arm maze used in the study.
mediolateral (ML), +2.1 mm from the midline; and dorsoventral (DV), −7.7 mm from the skull. After surgery, the rats received an intramuscular injection of penicillin-G procaine (0.2 ml, 20,000 IU) and were housed individually in plastic cages (30 cm × 19 cm × 12 cm) for 5 days, then returned to their home cages [12–14,19]. During the five days after surgery, in addition to water and food, 20% sucrose solution was provided ad libitum to prevent weight loss and reduce mortality [20,21].

2.4. The 5-arm maze test

Before evaluating sustained visuospatial attention in the rats, they were first trained in the basic task of making a rapid choice between the five open arms. The target arm with the light cue was baited with a reward and was changed pseudo-randomly from trial to trial. The aim of the first phase of the experiment was the rapid learning of the protocols of the task.

2.4.1. Habituation

One day before the training session, the rats were allowed free exploration and consumption of rewards in the 5-arm maze. The five arms were each baited with a chocolate pellet (Kellogg’s, Taiwan) as a reward, with the light on as a cue and the door open. The rat was placed in the start box with the transparent door open. After the rat left the start box, the sliding door of target box was closed and the rat explored the maze and visited the arms. When the rat left the visited arm, the light cue was turned off and the sliding door of that arm closed, resulting in the rat exploring all five baited arms. When all of the rat’s feet entered the arm, this was viewed as an entry. If the rat showed 60 s of non-exploration, it was gently pushed forward to reach an unsearched arm. The trial finished when all five arms had been explored.

2.4.2. Protocol of the training session

On the day after habituation, the rats started an 8-day training session for the acquisition of basic task in which they had to make a choice in each trial between the five open arms, only of which was illuminated and which changed from trial to trial. The first 4 days were called “training session 1” and the next 4 days were called “training session 2”. The rats received a daily training session, each composed of five trials, with a 30 min inter-trial interval.

The first trial of each daily session was called the “probe trial”, in which only one quasi-randomly selected arm, baited with a reward pellet and illuminated, was opened and used as the target arm. The probe trial was initiated with the rat in the start box. After a 10 second delay, the transparent sliding door of start box was opened and timing began when all four paws of the rat were outside the start box. When the rat entered the target arm, the illumination cue was turned off and the door was closed, and the latency was recorded. Entry into the open lit arm was rewarded by a food pellet.

In training session 1, in the other 4 trails on the same day, the rat was placed in the start box and all five arms were opened, with one quasi-randomly selected arm lit and baited with reward as the target arm and the other 4 arms unlit and containing no reward. After a 3 second delay, the sliding door of the start box was opened and timing started. Only a single arm choice was allowed in each trial; the door giving access to that arm was then closed, terminating the trial, the light was turned off, and the latency was recorded. A correct choice of the lit arm was rewarded by a food pellet. In “training session 2”, the only difference was that, when the rat put its head out of the box, the light cue in the target arm went on for only 2 s, instead of till the rat entered the arm.

2.4.3. Pre- and post-lesion tests

Both the pre- and post-lesion tests consisted of a 2-day session. Each session comprised five trials with a 30 min inter-trial interval and commenced with a probe trial.

The probe trial was initiated when the rat was placed in the start box. After a 3 second delay, the transparent sliding door of start box was opened and timing began once all 4 feet were outside the start box. Only one quasi-randomly selected arm baited with a reward pellet and lit for 2 s was opened when the rat put its head out of the start box. When the rat entered the target arm, the light cue was turned off and the door was closed and the latency was recorded. In the other four trials in this session, a quasi-randomly selected arm, baited with a reward and lit, was opened as the target arm. The other 4 arms were also opened, but no illumination and reward. The trial started when the rat was placed in the start box. After a 3 second delay, the start box sliding door was opened and, when the rat put its head out of the start box, the target arm was lit for 2 or 0.5 s. There is a negative correlation between the percentage of correct responses and cue duration [17]. It is difficult for an animal to make a correct response with a short cue duration and it will only perform well if it has very good attentional function. Thus, the percentage of correct response to cues of different duration has been used as an indication of performance of sustained visual attention in the test. Timing began as soon as all four of the rat’s feet were outside the start box. In this procedure, the rat was only allowed to approach one arm in each trial, then was removed from the maze. When the rat entered the arm, the arm was closed, the light was turned off, and the latency was recorded. After making a correct choice, the rat was removed from the box and given a chocolate pellet as a reward. A latency longer than 60 s was recorded as a failure response and the rat did not receive a reward.

2.5. Statistical analysis

All data are expressed as the mean ± S.E.M. The data for open field were analyzed using independent sample t-test. The data for the training session of the 5-arm maze test were analyzed using repeated measures analysis of variance (ANOVA). The data for the percentage of correct response on an indicated test day was analyzed using one-sample t-test or paired-samples t-test. The data in pre- and post-lesion tests were analyzed using the independent sample t-test or paired-samples t-test. For all comparisons, \( P < 0.05 \) was considered as significant.

3. Results

In the habituation phase, all the rats explored all five arms within 60 s.

3.1. Training session

The percentages of correct responses during the 8-day training session are shown in Fig. 2. Repeated measures of ANOVA revealed that during the training session, there was a gradual increase in the percentage of correct responses \( F(7,308) = 12.00, P < 0.001 \). The mean percentages of correct response were 34.4 ± 4.3% and 72.2 ± 3.7% for the first day and the last day of the training session, respectively. One-sample t-test revealed that all the percentages of correct response on the training days were significantly higher than that of 20% expected by chance (df = 44, all \( t \)-values > 8.00, all \( P \)-values < 0.001).

On the first day of training session 2, the percentage of correct responses showed a decline, compared to the data on the last day of training session 1 (paired-samples \( t \)-test, df = 44, \( t = 2.97, P = 0.005 \)).

3.2. Open field test

Motor function of the MPTP-lesioned and sham-operated rats in the open field test is shown in Table 1. No differences between the two groups were found in either the first 5 min or the next 5 min of testing.
3.3. Pre- and post-lesion tests in the 5-arm maze

The mean percentages of correct responses with a 2 or 0.5 second light cue in the pre- and post-lesion test phases are shown in Fig. 3.

In the pre-lesion test with a 2 second cue, there was no difference in the percentages of correct responses in the sham-operated (63.49 ± 5.8%) and MPTP-lesioned (62.5 ± 5.6%) rats. Using a 0.5 second light cue, there was again no difference (69.05 ± 4.5% and 62.5 ± 5.6%, respectively). No difference was observed between the percentages of correct responses using a cue duration of either 2 or 0.5 s in either group.

In the post-lesion test, when the cue duration was 2 s, there was no difference between the groups in the percentage of correct responses and neither group showed a difference between the pre- and post-lesion test results. However, when the cue duration was 0.5 s, the percentage of correct responses was significantly decreased in both groups (paired-samples t-test, df = 20, t = 3.35, P = 0.003 for sham-operated group; df = 22, t = 2.64, P = 0.015 for MPTP-lesioned group), compared to that seen with a cue duration of 2 s and there was no between-group difference.

4. Discussion

The principal aim of this study was to evaluate whether the MPTP-induced PD rats showed attentional deficits. The results showed that MPTP lesioning did not affect response accuracy in the sustained visuospatial attention task in the 5-arm maze, suggesting that the working memory impairment and object recognition deficits observed in PD animals [12–15] may not be due to an attentional problem. The 5-arm maze test used in the present study was adapted from that reported by Durkin et al. [17] for measuring visuospatial attention in mice. To examine the behavior of rats, we slightly modified the size of the maze and the test procedures. As far as we are aware, this is the first report measuring visuospatial attention in the PD rat model using the 5-arm maze test.

Durkin et al. [17] reported the use of the 5-arm maze test for mice. In the habituation and acquisition session in their study, the start box door was opened and the light cue turned on 10 s after the mouse was placed in the start box. However, in the habituation period in our study, the start box door was opened and all 5 arms were lit immediately after the rat was placed in the box. In the training session, the start box door was opened after a 10 second delay in the probe trial and after a 3 second delay in the choice trials. In training session 1, the target arm was lit until the rat entered an arm, while, in training session 2, the rat was placed in the start box, then 3 s later, the door was opened and the target arm was lit for only 2 s. Thus, the rat has enough time to find and run to the light target arm in training session 1, but only 2 s to detect the lit target arm in training session 2, and needed to pay more attention to the light cue.

One view of attention emphasizes the state of alertness or vigilance that enables animals to detect signals. In this view, attention is a generalized activation that attunes animals to all inputs. In another view, attention is a process that allows the selection of some sensory inputs from among many competing ones. Other investigators view attention as a “mental spotlight” that focuses on some stimuli, casting others in a “shadow” [22]. Thus, attention is responsible for selecting which stimulus to process and the selected information may then be memorized. Attention is required for the rats to detect the light cue in the 5-arm maze and underlies response accuracy. The present study demonstrated that PD animals showed a normal percentage of correct responses, indicating functional attention. We therefore suggest that the cognitive deficits seen in MPTP-lesioned rats in another behavioral test [12–15] may result from another cause, as there is a dissociation of neuronal mechanisms for attention, working memory, and recognition.

Table 1
Lack of effect of MPTP on behavior in the open field test.

<table>
<thead>
<tr>
<th></th>
<th>1–5 min</th>
<th></th>
<th>6–10 min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sham (n = 22)</td>
<td>MPTP (n = 24)</td>
<td>Sham (n = 22)</td>
</tr>
<tr>
<td><strong>Total distance (cm)</strong></td>
<td>1403.3 ± 66.4</td>
<td>1267.7 ± 80.7</td>
<td>809.8 ± 63.7</td>
</tr>
<tr>
<td><strong>Number of movements (no.)</strong></td>
<td>67.9 ± 1.9</td>
<td>69.6 ± 1.4</td>
<td>65.1 ± 2.6</td>
</tr>
<tr>
<td><strong>Rest time (s)</strong></td>
<td>130.6 ± 4.6</td>
<td>129.9 ± 4.9</td>
<td>81.1 ± 5.1</td>
</tr>
<tr>
<td><strong>Center time</strong></td>
<td>103.8 ± 7.2</td>
<td>123.1 ± 6.4</td>
<td>221.9 ± 4.8</td>
</tr>
</tbody>
</table>

Fig. 2. Changes in the percentage of correct responses in the 5-arm maze test during the 8-day training session. The percentage of correct responses is significantly higher than the chance level (20% dotted line) during the 8 training days. **P < 0.01, compared to the data for the last of training session 1.

Fig. 3. Effect of MPTP on the percentage of correct responses in the 5-arm maze test. On the day after the pre-lesion test, the rats underwent sham operation or MPTP lesioning, then, 10 days later, received the post-lesion test. *, P < 0.05, **, P < 0.01.
The 10 day delay between MPTP lesioning and the post-lesion test was decided on the basis of our previous studies, in which we found that, at 10 days after MPTP lesioning, the motor deficit had disappeared, but there was still a deficit of working memory in the T-maze test [12–15]. The gradual increase in the percentage of correct responses over the training session indicated that the rats successfully learned to connect a light cue and a food reward in the lit-target arm and to respond to the target arm. The maze was equipped with 5 arms and thus provided five possible choices. If no connection was made between light cue and reward, the percentage of correct responses would be that expected by chance, i.e. 20%. The percentages of correct responses in the training sessions were all significantly higher than chance, indicating that the rats learned to notice the light cue in order to make a correct response. Our data showed that the rats reached a level of 72.8% of correct responses in the 8-day training session. This is similar to that reported in C57BL/6 mice, which showed 75% of correct responses after 9 days of acquisition training [17]. It should be noted that there was a decline in the percentage of correct responses on the first day of training session 2 compared to the last day of training session 1; this was probably due to the shortening of the cue duration. In training session 1, the target arm was lit until the rat entered an arm, whereas, in training session 2, it was lit for only 2 s. Shortening of the cue duration causes a higher attentional load and might therefore result in a decrease in the percentage of correct responses. However, in the next 3 days of training session 2, the rats mastered the task and attained a higher percentage of correct responses.

Cognitive disorders observed in non-demented parkinsonian patients are frequent, but subtle, and mostly result from difficulties in controlling attentional resources. In particular, these deficits disturb the strategies involved in planning, as well as in encoding and retrieval processing of memory. In the pre-lesion test, none of the rats showed any difference in the percentage of correct responses when the cue was lit for either 2 s or 0.5 s. It should be noted that the performance of mice in the 5-arm maze was found to be a function of light cue duration, with the mice showing a lower percentage of correct responses with a shorter cue duration [17]. We, therefore, propose that the absence of a decline in the pre-lesion test in the percentage of correct responses with the 0.5 second light cue compared to the 2 second light cue may be due to a training effect, in which the rat learned to pay more attention to the shorter light cue [23]. After the pre-lesion test, the rats underwent sham operation or MPTP lesioning. Nine days after MPTP lesioning, no motor impairment was observed in the open field test, with no differences between MPTP-lesioned and sham-operated rats in terms of total distance, number of movements, movement time, rest time, or center time. Similarly, our previous study showed that MPTP lesioning caused transient motor dysfunction in the first few days after lesioning, as analyzed using the rotarod test, bar test, and open field test, then motor function recovered spontaneously within a week after lesioning [12–15]. Thus, the results of the behavioral tests in the present study were not confounded by motor deficits.

Ten days after MPTP lesioning, the rats received the post-lesion test and the results showed a decrease in the percentage of correct responses with a cue duration of 0.5 s compared to a cue duration of 2 s. This phenomenon was observed in both sham-operated and MPTP-lesioned groups. The decline in the percentage of correct responses with the shorter light cue allows an evaluation of the level of sustained visuospatial attention. Because the MPTP-lesioned and sham-operated rats showed the same percentage of correct responses with both a 2 second or 0.5 second cue, we propose that MPTP lesioning does not affect visuospatial attention in rats.

Attention, or selective attention, is the process of selecting, or focusing on, one or more stimuli for processing. The stimuli can come from the external environment or from an internal cognitive or somatic domain. The conscious selective component of this process acts like an attentional spotlight and can be endogenous (or voluntary) attention or exogenous (or reflexive) attention. Endogenous attention chooses which environmental stimuli to study and is directed toward aspects of the environment in keeping with interests and goals. Exogenous attention is that grabbed by external stimuli and is the involuntary reorienting of attention toward a stimulus source, cued by an object or event [24]. The light cue in the 5-arm maze test grabs the rat’s attention, and the rat can use this cue to decide which arm to respond to. This finding may be consistent with a report that patients with PDD have difficulty with internally cued behavior, but benefit substantially from external cues [25]. Furthermore, in the pre-lesion and post-lesion tests, there was a 3 second delay before the start box door was opened and the cue was lit and, to detect the light cue, the rats must pay sustained attention during this period.

We did not find any difference in performance in the 5-arm maze test between sham-operated and MPTP-lesioned rats. It should be noted that, due to the structural configuration of the maze, the position of the start box orients the rats such that they have a symmetrical view of the five arms. Since all 5 light cues were at the same distance in front of the rat and there were no differences in size, color, or texture of the cue, the 5-arm maze test may not measure the function of visuospatial recognition; however, the cues were at different locations, so the rat needed spatial ability to locate them. Analyzing the behavioral and cognitive features of MPTP-lesioned rats may help in understanding the neuropsychological changes and biochemical substrate underlying PD symptoms.

It has been reported that, after a 4-week test-free period, mice show a decrease in the percentage of correct responses in the 5-arm maze test [17]. However, in the present study a 10-day test-free period after surgery did not affect performance in the test using a 2 second light cue. This may indicate that long-term memory or consolidated reference memory was not affected by MPTP lesioning because, before surgery, the trained rats had established a long-term reference memory of the rule of the task, i.e. responding to the lit arm. In addition, the response latencies from the opening of the start box to entry into an arm of the MPTP-lesioned rats were as short as those of the sham-operated rats, in the range of 1–5 s (data not shown). The response latency was the time taken for the rat to run onto the central platform and select and enter an arm after the sliding door of the start box was raised. This also suggests that the running speed of MPTP-lesioned rats was not different from that of controls and supports our observations of the spontaneous recovery of motor function in the week after MPTP lesioning [12–16]. Furthermore, in almost all cases, the rats left the start box immediately after the door was opened and entered an arm. This shows that both groups of rats had a high level of motivation for searching for the reward in the 5-arm maze.

MPTP-lesioned rats are widely used as an animal model of PD. This animal model not only exhibits degeneration of the nigrostriatal system [26], but also exhibits PD symptoms [21,27–30]. The most prominent symptom in this model is motor dysfunction, which is observed in the first week after MPTP lesioning, but not later [12–15,21,28,31,32]. Furthermore, our previous studies demonstrated that the MPTP-lesioned rat PD model presents emotional and cognitive impairments, such as anxiety-like behaviors [14,19,33] and impairments of working memory [12,19], episodic-like memory [14], and object recognition [12,33]. Cognitive decline, one of the earliest non-motor features in PD, shows deficits in attention and working memory [34]. A previous study demonstrated that both the speed of image recognition and sustained attention are decreased in PD patients [25]. Although some PD patients show impairment of sustained visual attention, the impairment is associated with decreased object and space perception [36]. There are several aspects of attentional abilities, for example, visuospatial orienting, movement-switching, and sustained visual attention. PD patients show impairments in attentional set-shifting tasks [37] and sustained attention [35,36]. It would be interesting to know whether the deficit in attentional set shifting is also seen in the PD rat model.

In conclusion, as far as we are aware, this is the first study on visuospatial attention in the MPTP-induced PD rat model using the 5-arm.
maze test. Different tools and paradigms are needed to detect various aspects of attentional function in this model, and the results might provide data showing cognitive changes in DA degenerative disorders.

Acknowledgments

This work was supported by grants from the National Science Council of the ROC (NSC 102–2410-H-040-004, NSC 101–2410-H-040-003, and NSC 100–2923-H-040-009-MY3), and was partially supported by the grants from the budget from project No. 053 of the State Research Institute of Physiology and Fundamental Medicine SB RAMS. Conflicts of interest: The authors declare no conflicts of interest for the material in the manuscript.

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