Neuroscience Research xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Neuroscience Research

journal homepage: www.elsevier.com/locate/neures

Changes in efficiencies and interactions of attentional networks in Parkinson's disease with sleep disturbance

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ARTICLE INFO

Article history:
Received 20 December 2020
Received in revised form 30 April 2021
Accepted 10 May 2021
Available online xxx

Keywords:
Parkinson's disease (PD)
Attention
Sleep disturbance
Alerting
Orienting
Executive control

ABSTRACT

Attention is composed of three distinct attentional networks: alerting, orienting, and executive control. Previous studies have confirmed that Parkinson's disease (PD) is associated with executive control deficits; however, the interactions among the three attentional networks and the influence of sleep disturbance in PD patients have not been investigated. Herein, the efficiencies for the three attentional networks and their interactions were evaluated using the revised attention network test. The results showed a significantly slower response and lower accuracy in the PD group than in the normal control group and a significantly slower response and lower accuracy in PD patients with sleep disturbance (PDS) than in PD patients without sleep disturbance (PDnS), which indicates a response deficit in PD and worsening in PDS. Additionally, the executive control efficiency was reduced in both PDS and PDnS, and significantly higher alerting efficiency and lower orienting efficiency were found in PDS. Furthermore, largely changed interactions and correlation patterns of attentional networks were found in PDS but not in PDnS. These results suggested that attentional networks were impaired in PD patients, particularly in those affected by sleep disturbances, and that PDS might establish special connections between attentional networks to compensate for cognitive dysfunction.

1. Introduction

In Parkinson's disease (PD), nonmotor symptoms are common, in addition to prototypical cardinal motor features, such as resting tremors, bradykinesia, and rigidity (Barone et al., 2011). Cognitive disturbances are also extensively reported (Lou, 2009), including deficits in social cognition, abstract reasoning, memory, visuospatial attention, switching attention, and multisensory processing (Cagigas et al., 2007; Fearon et al., 2015; Ren, 2017; Ren et al., 2018; Sharpe, 1990b). Attention, as a major high-level cognitive function, is a complex system and is defined as a family of abilities that correctly allocate processing recourses to relevant events. However, both behavioral and event-related potential (ERP) studies have confirmed attentional deficits in PD patients, including mental switching (Cagigas et al., 2007; Inzelberg et al., 2001), distractor inhibition (Flowers and Robertson, 1985; Sharpe, 1990a), and selective attention (Hozumi et al., 2000; Vieregge et al., 1994).

Posner and Petersen proposed that attention is composed of three distinct attentional networks: alerting, orienting, and executive control (Petersen and Posner, 2012; Posner and Petersen, 1990). Sharpe (1990a,b) first reported that PD patients were more prone to distractor items than the normal control (NC) group (Sharpe, 1990a); a consistent result was also obtained by Cagigas et al. using a variant of the flanker task established by Eriksen and Eriksen (Cagigas et al., 2007), by which they proposed an impairment of executive attention in PD patients. Given that impairment of the basal ganglia is common in PD, Cagigas et al. further proposed that the basal ganglia might contribute to the interface of attention and action. To clarify whether deficits in executive control are accompanied by alterations in the alerting or orienting attentional networks in PD patients, Gravano and Jason (2012) examined the efficiencies of the three attentional networks simultaneously in PD patients using the attention network test (ANT) (Gravano

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https://doi.org/10.1016/j.neures.2021.05.004
0168-0102/

and Jason, 2012), which is widely used to assess attentional networks, including in healthy children (Rueda et al., 2004), children with attention deficit hyperactive disorder (Johnson et al., 2010), healthy older adults (Curran et al., 2001; Ishigami et al., 2015), PD patients (Cagigas et al., 2007; Pauletti et al., 2017; Vandenbossche et al., 2011; Zhou et al., 2012), neurocognitive disorder patients (Lu et al., 2016), essential tremor patients (Pauletti et al., 2015), and schizophrenia patients (Wang et al., 2005). Their results showed that PD patients illustrated a reduced P300 amplitude compared to that of the NC group, which showed significant impairment in executive attention but not in alerting attentional network and orienting attentional network (Gravano and Jason, 2012). A correlational study using the same experimental paradigm as that used by Zhou et al. found that although the alerting and executive control networks apparently remained unaffected, the efficiency of these attentional networks in PD patients was negatively correlated with the Hoehn & Yahr stage (Zhou et al., 2012), which suggested a possible deficit in the alerting effect and executive control of PD patients during the later stages. Studies have confirmed the interactions between the three attentional networks; therefore, deficits in one network can lead to alterations in other networks and their interactions (Fan et al., 2009; Petersen and Posner, 2012; Posner and Petersen, 1990). However, to our knowledge, whether the interactions are changed as the result of deficits in alerting or executive attentional networks in PD patients has still not been investigated. Understanding the efficiencies of the three attentional networks and their interaction are the keys to fully clarifying the declining mechanism of attention processing for PD patients. Based on the original ANT, Fan et al. optimized the attentional contrasts and developed the revised attentional network test (ANT-R), which makes it possible to simultaneously examine the interactions between the three attentional networks (Fan et al., 2009). Therefore, in the current study, the ANT-R was conducted to evaluate the efficiencies of the three attentional networks and their interactions in PD patients. Given the overlapping processes of the three attentional networks, we hypothesized that the interactions between the three attentional networks would be changed compared with those of the NC group.

Furthermore, a recent study reported that other nonmotor symptoms of PD also greatly affect attentional network efficiency (Pauletti et al., 2017). Pauletti et al. assessed the effect of fatigue on PD patients' attentional network using ANT, and their results showed lower executive network efficiency in PD patients with fatigue than in PD patients without fatigue, which suggested that fatigue might contribute to worse executive dysfunction in PD patients (Pauletti et al., 2017). Sleep disturbances are common nonmotor symptoms that occur in 60–98 % of PD patients and are an important factor that results in fatigue (Suzuki et al., 2015; Swick, 2012). In addition, the prevalence of sleep disturbances increases in parallel with disease progression (Davie, 2008; Swick, 2012; Swick and Ondo, 2016), and they can occur at any point in the disease course, even at the initial stage of PD patients (Avidan et al., 2013; Swick, 2012). Studies have confirmed that PD-related pathological changes also contribute to the occurrence of sleep disturbances (Suzuki et al., 2015). However, because no investigation has focused on the effect of sleep disturbance on attentional networks in PD patients, it is still unknown whether sleep disturbance influences the interactions and correlations between attentional networks. Therefore, in the current study, PD patients were divided into two groups, PD patients with sleep disturbance (PDS) and PD patients without sleep disturbance (PDnS), to further investigate the effect of sleep disturbance on efficiencies and interactions between attentional networks. Considering that sleep disturbances contribute to fatigue and fatigue worsens executive dysfunction (Pauletti et al., 2017; Suzuki et al., 2015), we hypothesized that the attentional networks would be deteriorated in PDS compared with those of PDnS. Additionally, although cognitive functional decline occurs in PDS, they can still complete many cognitive tasks; therefore, we further hypothesized that the interactions between the attentional networks would be changed in PDS.

Table 1
Demographics of NC and PD participants.

	NC	PDnS	PDS
H&Y stage	NA	2.4(0.1)	2.7(0.2)
Disease Duration*	NA	3.1(0.7)	6.7(1.4)
Education	12.5(0.5)	12.3(0.5)	12.6(0.5)
PDSS-2***	9.5(1.2)	7.8(0.8)	20.0(2.1)
ESS*	5.1(1.0)	5.0(1.1)	8.6(1.1)
PSQI**	5.1(0.6)	4.1(1.0)	8.7(1.4)
MOCA	27.6(0.4)	24.6(0.5)	23.5(0.6)
LED (mg/day)	NA	429(81)	515(65)

Data are presented as the mean ± standard error of the mean (SEM). *$p \leq 0.05$, **$p \leq 0.01$, and ***$p \leq 0.001$ indicates a statistically significant difference between the PDnS and PDS groups.

2. Methods

2.1. Subjects

The sample size was calculated using the G*Power 3.1.9.2 program[2] ; the total sample size was 60, with an effect size *f* of 0.25 and a power (1-β err prob) of 0.95. Therefore, twenty healthy older participants (63–78 years, mean age ± SD, 70.3 ± 1.0), 20 PDnS (58–75 years, mean age ± SD, 68.9 ± 1.4), and 20 PDS (59–74 years, mean age ± SD, 70.7 ± 1.5) participated in this study. Healthy older participants who made up the NC group were randomly recruited from the Okayama Silver Human Resources Center, and all healthy older participants were age-matched with PD patients and paid 1000 yen per hour. All PD patients were recruited from outpatient clinics at the Department of Neurology, Dokkyo Medical University Hospital. All NC and PD participants agreed to participate in the current experiment and completed the experiment successfully. The diagnosis of PD was made by board-certified neurologists according to the established criteria (Hughes et al., 1992), and the disease duration for PD patients is recorded in Table 1. All participants were naïve to the device and task and provided written informed consent to participate in the study, which was previously approved by the ethics committee of Okayama University (healthy participants) or of Dokkyo Medical University Hospital (PD patients) according to the location at which the experiment was performed. Additionally, all NC participants were in good physical condition and reported not taking any medications that might have central nervous system effects.

2.2. Materials

2.2.1. Questionnaire assessment session

The overall cognitive function of each participant was assessed using the Montreal Cognitive Assessment (MOCA), and the subject was defined as having a cognitive deficit if his or her MOCA score was lower than 26 (Fujiwara et al., 2010). Sleep was assessed using the Japanese versions of the Parkinson's Disease Sleep Scale-2 (PDSS-2) (Suzuki et al., 2012), the Pittsburgh Sleep Quality Index (PSQI) (Doi et al., 2000), and the Epworth Sleepiness Scale (ESS) (Johns, 1991; Takegami et al., 2009). The subject was defined as a poor sleeper if he or she had a global PDSS-2 score ≥ 15 (Suzuki et al., 2012), as having insomnia if his or her overall PSQI score was ≥ 6 (Buysse et al., 1989), and as having excessive daytime sleepiness

[2] http://stats.idre.ucla.edu/other/gpower/

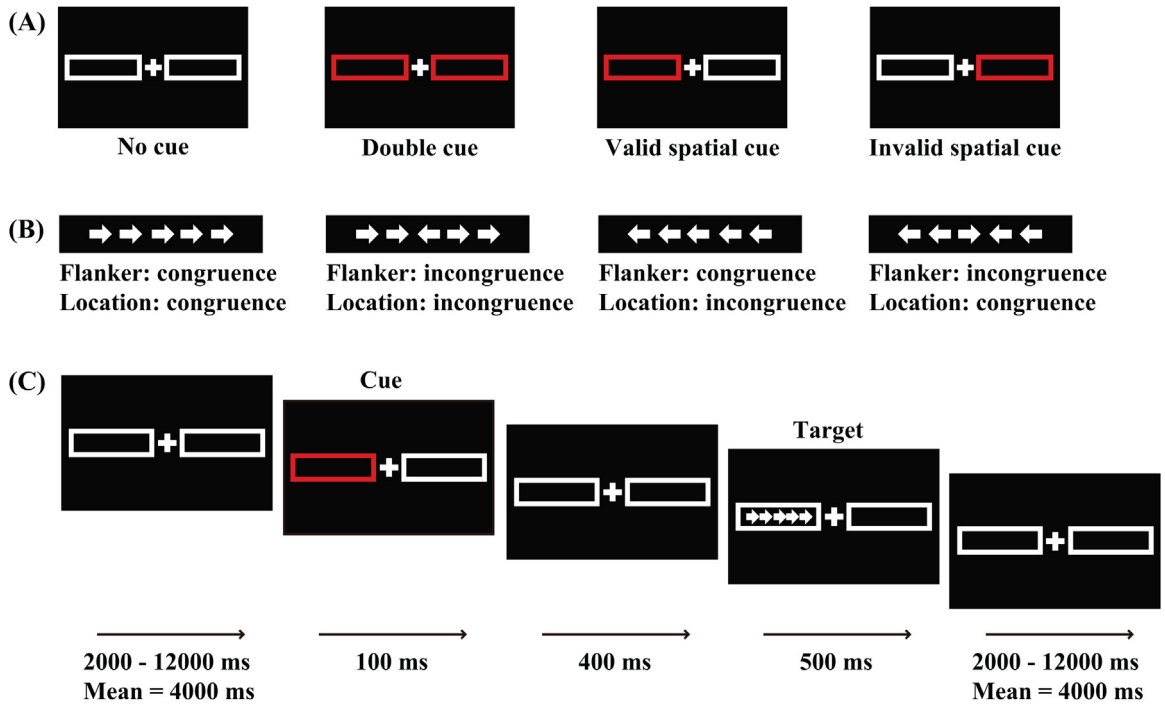

Fig. 1. Description of the experimental paradigm for the attention network test. (A) Four cue conditions. (B) Four target conditions. (C) An example of a stimulus used to form a possible trial sequence in the experiment.

if he or she had a total ESS score ≥ 11 (Johns, 1991). Additionally, for PD patients, disease severity was rated using Hoehn and Yahr (H&Y) staging (Hoehn and Yahr, 1998), and the disease duration and levodopa equivalent dose (LED) used were obtained from the attending physician with the patient's permission.

2.2.2. Attentional network test session

The ANT-R was adapted from Jan et al. (Fan et al., 2009). To ensure that the PD patients completed the experiment successfully, the experimental protocol was optimized by altering the presentation time of the stimulus and the inter-stimuli interval with the assistance of their attending physician according to previous studies (Cagigas et al., 2007; Pauletti et al., 2017; Vandenbossche et al., 2011; Zhou et al., 2012) and the actual physical condition of PD patients. The visual targets consisted of a row of 5 horizontal black arrows with one central target plus four flankers, two on each side (Fig. 1B). All of the white arrows pointed either left or right against a black background. Each single arrow subtended 0.58 degrees of the visual angle, and two adjacent arrows were separated by a gap of 0.06 degrees of the visual angle. Therefore, an entire stimulus including the five arrows subtends a total of 3.27 degrees of the visual angle (target + flanker array). The visual cue was a flashing red box, which was shown before the presentation of the target. When the cue appeared, it may or may not have assisted the participants in detecting the subsequent target depending on the cue condition. There were four types of cue conditions (Fig. 1A): no cue condition (no white cue box flashed red before the target appears, 1/6), a double cue (both white cue boxes flashed red before the target appeared so that the cue was only temporally informative, 1/6), an invalid spatial cue (one of the white cue box flashed red before the target appeared, but the following target was presented in the contrary location so that the cue was temporally informative and spatially uninformative, 1/6), and a valid spatial cue (one of the white cue box flashed red before the target appeared and the following target was presented in the same location so that the cue was temporally and spatially informative, 3/6). During the experiment, all of the visual targets and cues were presented 4.69 degrees to the left or right of the fixation on a black background on a 21-inch computer monitor positioned 60 cm in front of the participant's eyes.

2.3. Experimental procedure

2.3.1. Questionnaire assessments session

The questionnaire assessments were conducted in the outpatient department or in a special quiet room with the assistance of professional staff in random order according to the location at which the examination was performed. This session lasted approximately 40 min.

2.3.2. Attentional network test session

Subjects were instructed to conduct an attention network test in a quiet room (a laboratory room at Okayama University or at Dokkyo Medical University Hospital, Japan dependently) with their eyes fixed on the fixation cross (Fig. 1C). In each trial, depending on the cue condition (no, double, and valid or invalid cues), a white cue box flashed red for 100 ms. After 400 ms, the visual target was presented for 500 ms. Participants were instructed to identify the direction of the center arrow by pressing the left button of the mouse for a left direction and the right button otherwise as accurately and quickly as possible based on their handedness, while ignoring the location and flanker direction (left or right) of the target relative to the fixation cross (Fig. 1C). The ratio for the no cue, double cue, invalid cue and valid cue tasks was 1:1:1:3; for the congruence and incongruence tasks, the ratio was 1:1 for both flanker congruency and location congruency. In the no cue, double cue and invalid cue conditions, there were 6 trials for each kind of trial presented on the left or right hemisphere of the screen in pseudorandom order to avoid the same stimulus type appearing in succession. In the valid cue condition, there were 18 trials for each kind of trial. The intertrial interval varied randomly (18 times for each interval from 2000 to 5000 ms with an increasing step of 500 ms and 18 trials for 10,500 ms). In all, the formal experiment included 144 trials and was divided into 4 blocks. To ensure the

Table 2
Calculation of attentional network efficiency and interactions.

	Testing condition	*Minus*	Reference condition
Network effects			
Alerting	No cue		Double cue
Orienting	Double cue		Valid cue
Validity	Invalid cue		Valid cue
Conflict	Incongruent		Congruent
Interactions			
Alerting	No cue, incongruent		Double cue, incongruent
by	*Minus*		*Minus*
Executive control	No cue, congruent		Double cue, congruent
Orienting	Double cue, incongruent		Valid cue, incongruent
by	*Minus*		*Minus*
Executive control	Double cue, congruent		Valid cue, congruent
Validity	Invalid cue, incongruent		Valid cue, incongruent
by	*Minus*		*Minus*
Executive control	Valid cue, congruent		Valid cue, congruent

This table was reproduced from Jan's publication (Fan et al., 2009).

availability of data, before the formal experiment, a practice session was performed until the accuracy was greater than 90 %, and each trial was followed by feedback to instruct the participants on how to respond to the target. However, in the formal experiment, feedback was only given after the block was finished to tell the participant the number of correct trials. The attention network test session lasted approximately 40 min overall.

2.4. Data analysis

2.4.1. Questionnaire assessments

The global score was computed separately for each subject for each questionnaire assessment, and the data were subjected to one-way ANOVA. Additionally, *t-tests* (two-tailed) were conducted to analyze differences in the disease duration, the H&Y stage, and the LED between the PDnS and PDS groups. The statistical significance level was set at $p \leq 0.05$.

2.4.2. Cueing effect assessment

According to a previous study, the trials in which the response time (RT) was less than 200 ms (anticipation) or longer than 1700 ms (omission) were excluded by the task program, and we did not exclude further outliers with any other method (Fan et al., 2009). The mean RT and accuracy (ACC) for each condition were calculated separately, and then the data were subjected to 3_{Groups} (NC, PDnS, PDS) × 4_{CueTypes} (no cue, double cue, valid cue, invalid cue) ANOVA (Greenhouse-Geisser corrections with corrected degrees of freedom). The statistical significance level was set at $p \leq 0.05$, and the effect size (η_p^2) estimates were also reported.

2.4.3. Attentional network efficiency and its interaction

The attentional network efficiency was calculated based on the RT difference in response to different cue-type targets, by which the different effects of motor function between groups were removed (Table 2). The significance of attentional network efficiency and its interaction was calculated using *t-tests* (two-tailed), and the group diversity in each attentional network effect was tested using separate one-way ANOVAs. The strength and direction of the linear relationships between attentional networks was tested using Pearson's correlation analysis. The statistical significance level was set at $p \leq 0.05$.

3. Results

3.1. Questionnaire assessment

One-way ANOVA showed no significant differences among the groups in education (all $p = 1.000$) and age (all $p \geq 0.083$), which indicated that the NC group met the criteria of a control group and that it was also reasonable to investigate PDS based on PDnS. For the PDSS-2 scores, there were significant differences between PDS and the NC group ($p < 0.001$) and between PDS and PDnS ($p < 0.001$) but not between the NC group and PDnS ($p = 1.000$). For the ESS and PSQI scores, a significant difference was found between PDS and PDnS (all $p \leq 0.045$) but not between the NC group and PDS (all $p \geq 0.056$) or the NC group and PDnS (all $p = 1.000$). The statistical results for PDSS-2, ESS, and PSQI showed significant sleep disturbance for the PDS group. For the MOCA scores, there were significant differences between the NC group and PDnS ($p < 0.001$) and the NC group and PDS ($p < 0.001$) but not between PDnS and PDS ($p = 0.424$), which indicated significant cognitive decline for PD patients. *T-test* (two-tailed) analysis showed a significant difference in disease duration ($p = 0.016$) between PDS and PDnS but not in the H&Y stage or LED.

3.2. Cueing effect assessment

3.2.1. Mean response time

The mean RTs for NC and PD patients are shown in Fig. 2A. The 3_{Goups} (NC, PDnS, PDS) × 4_{CueType} (double cue, invalid cue, no cue, valid cue) ANOVA showed a significant main effect of group [$F(2, 57) = 8.673$, $p < 0.001$, $\eta_p^2 = 0.233$], which indicated the fastest response to the target by the NC group (NC > PDnS > PDS). A main effect of cue type [$F(3, 171) = 283.849$, $p < 0.001$, $\eta_p^2 = 0.833$] showed the fastest response to valid cue trials compared to double cues, invalid cues and no cue trials (valid cue > double cue > no cue > invalid cue). Additionally, a significant interaction between the group and cue type [$F(6, 171) = 4.587$, $p < 0.001$, $\eta_p^2 = 0.139$] was also found. Further *post hoc* analysis for the group was conducted. In the NC group, the paired comparison showed that there were significant differences among the double cue, invalid cue, no cue and valid cue trials (all $p \leq 0.003$), with the exception of the invalid cue and no cue trials ($p = 0.290$). In the PDnS group, the paired comparison showed significant differences among the double cue, invalid cue, no cue and valid cue trials (all $p \leq 0.002$), with the exception of the invalid cue and no cue trials ($p = 0.120$). In the PDS group, the paired comparison showed significant differences among all four cue types (all $p < 0.001$). *Post hoc* analysis for cue types was also conducted. The paired comparison showed that under all four cue-type conditions (double cue, invalid cue, no cue and valid cue), there were significant differences between the NC group and PDS ($p \leq 0.005$), but there were no significant differences between the NC group and PDnS ($p \geq 0.203$). Significant differences were found between PDnS and PDS under invalid cue and no cue conditions ($p \leq 0.033$) but not under double cue or valid cue conditions ($p \geq 0.282$).

3.2.2. Mean ACC

The mean ACC for NC and PD patients are shown in Fig. 2B. The 3_{Goups} (NC, PDnS, PDS) × 4_{CueType} (double cue, invalid cue, no cue, valid cue) ANOVA showed a significant main effect of group [$F(2, 57) = 5.259$, $p = 0.008$, $\eta_p^2 = 0.156$], with the highest accuracy for the NC group and the lowest accuracy for PDS (NC > PDnS > PDS, all $p < 0.018$). Additionally, a significant main effect of cue type [$F(3, 171) = 4.254$, $p = 0.010$, $\eta_p^2 = 0.065$] was found, with a higher accuracy for the valid cue condition. However, no other main effect or interaction was found (all $p \geq 0.05$); therefore, the analysis of attentional network efficiency and its interaction was calculated using RT but not ACC.

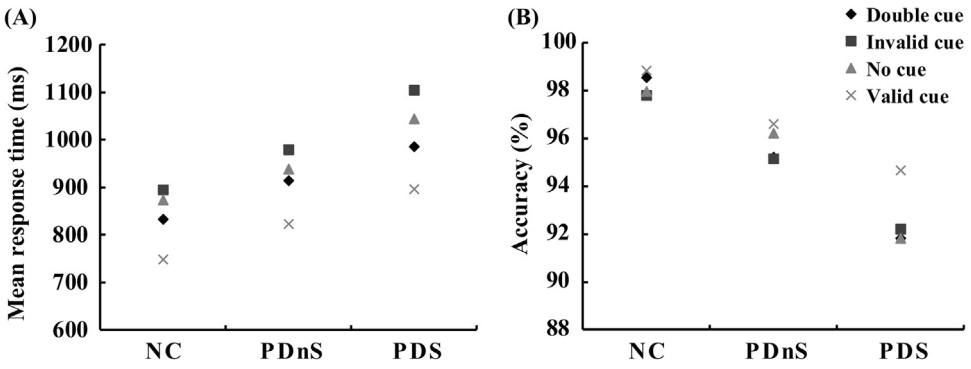

Fig. 2. Response (A) was significantly faster and accuracy was significantly higher (B) in the NC group than in PDnS and PDS (NC > PDnS > PDS).

3.3. Attentional network efficiency

All efficiencies of the attentional networks were calculated according to Table 2, and the results are summarized in Table 3.

3.3.1. Alerting effect

The comparison of the RTs between the double cue and no cue conditions showed significant benefit in RTs related to the double cue, which was 41 ± 39 (mean ± SD) for the NC group ($p < 0.001$), 26 ± 55 for the PDnS group ($p = 0.005$), and 59 ± 48 for the PDS group ($p < 0.001$) (Table 3). One-way ANOVA showed significant differences in alerting between the PDS and NC ($p = 0.033$) groups and between the PDS and PDnS ($p = 0.024$) groups, but there was no significant difference found in alerting between the NC and PDnS groups ($p = 0.089$), which indicated similar alerting efficiency in the NC and PDnS groups but much higher alerting network efficiency in PDS.

3.3.2. Orienting effect

The orienting effect was assessed by validity, disengaging, and moving + engaging. For validity, the comparison of RTs between the invalid cue and valid cue conditions showed significant benefit in RTs related to the valid cue, which was 147 ± 56 for the NC group ($p < 0.001$), 156 ± 59 for the PDnS group ($p < 0.001$), and 208 ± 58 for the PDS group ($p < 0.001$) (Table 3). One-way ANOVA showed that there were significant differences in validity between the PDS and NC groups ($p = 0.005$) and between the PDS and PDnS groups ($p = 0.015$), but there was no significant difference between the PDnS and NC groups ($p = 1.000$). For disengaging, the comparison of RTs between the invalid cue and double cue conditions showed significant benefit in RTs related to the double cue, which was 62 ± 45 for the NC group ($p < 0.001$), 69 ± 46 for the PDnS group ($p < 0.001$), and 115 ± 44 for the PDS group ($p < 0.001$) (Table 3). One-way ANOVA showed that there was a significant difference in disengaging between the PDS and NC groups ($p = 0.001$) and between the PDS and PDnS groups ($p = 0.001$), but there was no significant difference between the PDnS and NC groups ($p = 1.000$). For moving + engaging, the comparison of RTs between the double cue and valid cue conditions showed significant benefit in RTs related to valid cues, which was 85 ± 28 for the NC group ($p < 0.001$), 91 ± 34 for the PDnS group ($p < 0.001$), and 90 ± 48 for the PDS group ($p < 0.001$) (Table 3). One-way ANOVA showed no significant difference in moving + engaging among the three subgroups (all $p = 1.000$). These results indicated that there was no significant difference in the orienting network efficiency in the NC and PDnS groups; however, it was reduced in the PDS group.

3.3.3. Executive control effect

The executive control effect was assessed by flanker conflict and location conflict. For flanker conflict, the comparison of RTs between the flanker congruent and flanker incongruent conditions showed significant benefit in RTs related to flanker congruency, which was 130 ± 42 for the NC group ($p < 0.001$), 186 ± 93 for the PDnS group ($p < 0.001$), and 193 ± 96 for the PDS group ($p < 0.001$) (Table 3). One-way ANOVA showed a significant conflict difference between the NC and PDnS groups ($p = 0.017$) and between the NC and PDS groups ($p = 0.005$) but not between the PDnS and PDS groups ($p = 1.000$). These results indicated executive control deficits in PDnS and PDS. However, a significant location benefit was found in PDS ($p = 0.039$) but not in PDnS and the NC group (all $p > 0.05$), which further indicated much worse executive control in PDS.

3.4. Interactions between attentional networks

All of the interactions between attentional networks (Table 3) were calculated according to Table 2, and then the data were submitted to *t-tests* (two-tailed).

3.4.1. Alerting by executive control

A significant interaction between alerting and flanker conflict was found for the NC (-3 ± 5 ms, $p = 0.027$), PDnS (23 ±68 ms, $p = 0.014$), and PDS groups (8 ±102 ms, $p = 0.017$); however, no significant interaction between alerting and location conflict was found for the NC (−14 ± 34 ms, $p = 0.086$), PDnS (−20 ± 63 ms, $p = 0.176$), or PDS groups (−39 ± 99 ms, $p = 0.089$) (Table 3). These results indicated that the alerting effect hindered flanker conflict processing in the NC group but facilitated flanker conflict processing in the PDnS and PDS groups.

3.4.2. Orienting by executive control

A significant interaction between orienting and flanker conflict was found for the NC (20 ± 49 ms, $p = 0.049$), PDnS (−37 ± 91 ms, $p = 0.028$), and PDS groups (−22 ± 88 ms, $p = 0.003$) (Table 3), which indicated that orienting facilitated flanker conflict processing for the NC group but hindered flanker conflict processing for PDnS and PDS. In addition, a significant interaction between validity and flanker conflict was found for the NC (22 ± 51 ms, $p = 0.027$), PDnS (−82 ± 379 ms, $p = 0.035$) and PDS (−30 ± 59 ms, $p = 0.003$) groups, which indicated that invalid cues hindered flanker conflict processing for the NC group but had the inverse effect for the PDnS and PDS groups.

The analysis for the interaction between orienting and location conflict revealed a significant interaction for the PDS group (33 ± 108 ms, $p = 0.017$) but not for the NC (4 ± 33 ms, $p = 0.615$) and PDnS groups (−10 ± 43 ms, $p = 0.292$), which indicated that orienting facilitated location conflict processing for the PDS group. In addition, a significant interaction between validity and location conflict was found for the NC (20 ± 38 ms, $p = 0.034$), PDnS (12 ± 46 ms, $p = 0.026$), and PDS groups (46 ± 75 ms, $p = 0.002$), which

Table 3
The efficiency of attentional networks and their interactions (ms) with standard deviation (SD).

	NC		PDnS		PDS	
	Mean	SD	Mean	SD	Mean	SD
Alerting	41***	39	26*	55	59***	48
Validity	147***	56	156***	59	208***	58
Disengaging	62***	45	65***	46	119***	44
Moving + Engaging	85***	28	91***	34	90***	48
Flanker Conflict	130***	42	186***	93	193***	96
Location Conflict	−6	28	−12	29	−16*	40
Flanker*Location	−9	50	−15*	28	13*	67
Alerting*Flanker	−3*	55	23*	68	8*	102
Orienting*Flanker	20*	49	−37*	91	−22*	88
Validity*Flanker	22*	51	−82*	379	−30**	59
Alerting*Location	−14	34	−20	63	−39	99
Orienting*Location	4	33	−10	43	33*	108
Validity*Location	20*	38	12*	46	46**	75

* $p \leq 0.05$.
** $p \leq 0.01$.
*** $p \leq 0.001$.

indicated that invalid cues hindered location conflict processing for all subgroups.

3.4.3. Flanker by location conflict

A significant interaction between flanker and location conflict was found in the PDnS (-15 ± 28 ms, $p = 0.029$) and PDS (13 ± 67 ms, $p = 0.039$) groups but not in the NC group (-9 ± 50 ms, $p = 0.423$) (Table 3), which showed that the flanker congruent effect is greater under the congruent location condition than under the incongruent location condition for the PDnS group but inverse for the PDS group.

3.5. Correlations between attentional networks

The correlation coefficients for attentional network effects and significance are shown in Table 4. For the NC group, significant positive correlations were mainly found among validity and other attentional effects, such as disengaging (r = 0.763, $p = 0.004$), moving + engaging (r = 0.642, $p = 0.004$), and location conflict (r = 0.529, $p = 0.037$). A significant positive correlation between alerting and flanker conflict (r = 0. 588, $p = 0.009$) and a negative correlation between alerting and moving + engaging (r = −.0.368, $p = 0.047$) were also found. For the PDnS group, except for the correlations that were similar to those of the NC group, the correlation between alerting and flanking changed from a positive correlation (r = 0.588, $p = 0.009$) to a negative correlation (r = −0.505, $p = 0.042$), which indicated that some problems occurred when solving conflict in the PDnS group. In addition, significant positive correlations between moving + engaging and flanker conflict (r = 0.860, $p = 0.008$) and flanker conflict and location conflict (r = 0.462, $p = 0.003$) were found in the PDnS group, which were absent in the NC group. For the PDS group, and different from the NC and PDnS groups, the correlations among disengaging and other attentional effects were established extensively, including alerting (r = 0.576, $p = 0.007$), validity (r = 0.676, $p = 0.005$), moving + engaging (r = −0.734, $p = 0.004$), flanker conflict (r = −0.456, $p = 0.045$), and location conflict (r = 0.485, $p = 0.008$). In both the NC and PDnS groups, no correlation between disengaging and other attentional effects was found, which indicated that the PDS group might have a serious disengaging system deficit. Similar to the PDnS group, there were also correlations among moving + engaging and alerting (r = −0.451, $p = 0.034$) and flanker conflict (r = 0.659, $p = 0.012$).

4. Discussion

The executive control efficiency was reduced in both the PDS and PDnS groups compared with that of the NC group, which was consistent with previous studies (Cagigas et al., 2007; Gravano and Jason, 2012; Pauletti et al., 2017; Sharpe, 1990b). Conflict resolution impairment has been widely reported in PD, even in early stages (Pauletti et al., 2017; Vandenbossche et al., 2011, 2012). The executive network is responsible for conflict resolution, error detection and inhibitor control (Petersen and Posner, 2012; Posner and Petersen, 1990). A functional neuroimaging investigation demonstrated that the executive network involves the anterior cingulate cortex and lateral prefrontal cortex and that there are large numbers of dopamine receptors in these regions (Roca et al., 2011). Dopamine depletion is common in PD patients, which might be the main reason for the lower executive network efficiency.

In addition, much higher alerting network efficiency and lower orienting efficiency were found in PDS. It is known that sleep disturbance leads to more serious daytime fatigue (Pauletti et al., 2017), depression (Benzagmout et al., 2019), and attention deficits (Suzuki et al., 2015; Swick, 2012; Zhou et al., 2012). Pauletti et al. investigated the influence of fatigue on attentional networks in PD, and their results showed a slower response to the target in PD with fatigue than in PD without fatigue (Pauletti et al., 2017). Therefore, fatigue created by sleep disturbance may lead to a worse response in PDS. In addition, the basal ganglia are involved in emotion processing, and positive emotions activate relatively larger volumes of the same anatomical entities than neutral and negative emotions (Benzagmout et al., 2019). Studies have also shown that emotion can affect perceptual ability to a great degree: a positive emotion can enhance the synthesis and release of dopamine and assist in precisely perceiving stimuli (Cawley et al., 2017). Therefore, the depression created by sleep disturbance and basal ganglia damage might also contribute to a worse response in PDS. Furthermore, there is a much more severe loss of noradrenergic input from the locus coeruleus to cortical regions in PD patients with dementia than in those without dementia (Chan-Palay and Asan, 1989). In the current study, although there was no significant difference in the MOCA scores between PDnS and PDS, the mean MOCA score for PDS (23.5) was lower than that for PDnS (24.6). Because dopamine and noradrenaline are involved in the control of sleep, we proposed that noradrenergic involvement may also be related to a worse response in PDS than in PDnS. In the current study, the participant was instructed to make a faster and more accurate response. Because of the functional decline resulting from the internal factor, the PDS needed to rely much more on external alerting cues to

Table 4
Correlation coefficients among attentional network effects for NC, PDnS and PDS groups.

	Alerting	Validity	Disengaging	Moving + Engaging	Flanker conflict
NC					
Alerting					
Validity	.004				
Disengaging	.351	.763**			
Moving + Engaging	−.368*	.642**	−.006		
Flanker conflict	.588**	.096	.133	−.009	
Location conflict	−.110	.529*	.455	.278	.089
PDnS					
Alerting					
Validity	−572				
Disengaging	.257	.540**			
Moving + Engaging	−.700**	.772**	−.432		
Flanker conflict	−.505*	.765	−.227	.860**	
Location conflict	−.289	.468**	.042	.221	.462*
PDS					
Alerting					
Validity	.359				
Disengaging	.576**	.676**			
Moving + Engaging	−.451*	.006	−.734**		
Flanker conflict	.266	−.390	−.456*	.659*	
Location conflict	−.040	.335	.485*	−.349	.700**

* $p \leq 0.05$.
** $p \leq 0.01$.

be able to make an appropriate motor response, exhibiting much higher external alerting. Additionally, orienting from one target to another presented in an opposite location involves many steps, such as perception of the new target, disengaging attention from the present target, moving attention, and engaging attention on the new target. Slowing in any step will reduce the orienting efficiency. As depression can easily affect one person's physiological state, it is possible that depression interferes with the orientation of steps. Therefore, we proposed that the reduced orienting efficiency might also be mainly attributed to depression created by sleep disturbance.

Additionally, the interaction between alerting and flanker conflict was altered from negative for the NC group to positive for the PD patients. A previous study showed that alerting and executive processes occurred in parallel and that the two cognitive actions were completed with the same attentional resolution (Fan et al., 2009, 2002). The attentional load theory proposed by Lavie states that if limited cognitive resources are allocated to one cognitive process to a greater degree, the other process will have fewer resources (Lavie and Tsal, 1994); therefore, there is a negative effect on executive control in the NC group. Cognitive dysfunction was significant in PD in the current study ($p < 0.01$) and may lead to disability in simultaneously monitoring and programming the response to the target. Therefore, we proposed that in PD patients, the alerting system was activated first to assist in subsequent target detection and discrimination (Petersen and Posner, 2012), which showed a positive correlation between alerting and executive control in PD. In addition, the interaction between orienting and validity was altered from positive for the NC group to negative for PD patients. The fact that orienting to the target location in advance enhances the response and reduces conflict is easy to understand. There is also no doubt that valid orienting speeds up the response and invalid orienting delays the response. Therefore, it is reasonable for the NC group to have positive orienting and validity effects on flanker conflict. Orienting and executive control share some brain regions, and both cognitive processes require a division of attentional resources (Fan et al., 2009; Lavie and Tsal, 1994). According to attentional load theory, when the two tasks are simple to carry out, they can be easily completed, and facilitation will occur if they are related to each other (Lavie and Tsal, 1994). For PD, the cognitive deficits were significant compared to those of the NC group in the present study ($p < 0.01$). The same task will be more difficult in PD patients than in the NC group (Fig. 2B, $RT_{NC} < RT_{PD}$; $ACC_{NC} > ACC_{PD}$). Consistent with attentional load theory, orienting and executive control compete for shared attentional resources, which leads to a negative effect.

Furthermore, positive orienting by location and flanker by location interactions occurred in PDS but were absent in the NC group and PDnS. A possible reason might be the visual angle at which the target was presented (4.69 degrees). The processing speed to the same target largely depended on the visual angle of the target presented, and the processing was faster when it was presented at the central location than at the peripheral location (Wang et al., 2016; Fearon et al., 2015). The visual field decreased with aging and was only 52 % of the size of a 20-year-old central field compared to 60-year-old central field (WILLIAMS, 1983). In addition, previous studies have shown that posterior cortical atrophy is widely reported in PD patients with cognitive decline, which leads to a narrow visual field and visual processing dysfunction (Armstrong, 2017; Lehmann et al., 2011). For the NC and PDnS groups, the visual angle of 4.69 degrees is central, and it was easy to process the spatial diversity; however, in the PDS group, the visual angle is relatively psychophysically larger, resulting from sleep disturbance and cognitive dysfunction, which leads to PDS relying more on a congruent location. In addition, it is noteworthy that the correlations changed slightly in PDnS, but the correlation pattern changed greatly in PDS, as the correlation with disengaging widely occurred with alerting (r = 0.576), validity (r = 0.676), moving + engaging (r = −0.734), flanker conflict (r = −0.456), and location conflict (r = 0.485). Together with the diversity of network efficiency between PDS, the NC group and PDnS, we proposed that to complete the task and to solve problems in life, PDS establish more interactions with other networks to compensate for cognitive dysfunction and lower attentional network efficiency in executive control. However, to clarify these compensatory mechanisms, further neuroimaging studies are needed.

5. Conclusion

Compared with the NC group, the executive control efficiency was significantly reduced in both PDS and PDnS. Additionally, the alerting efficiency was significantly higher and the orienting efficiency was significantly lower in PDS but not in PDnS. Furthermore,

the interactions between different attentional networks and their correlations were largely altered in PDS.

Data availability

The data is available from the corresponding author on reasonable request.

Funding statement

The study was partially supported by the National Natural Science Foundation of China (31800932, 31700973), the Science and Technology Planning Project of Guizhou Province (QianKeHeJiChu-ZK [2021] General 120), the Innovation and Entrepreneurship Project for High-level Overseas Talent of Guizhou Province [(2019)04], and the Humanity and Social Science Youth Foundation of the Ministry of Education of China (18XJC190003).

Declaration of Competing Interest

All of the authors declare that they have no potential conflicts of interest to disclose.

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