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Attention network impairments in patients with focal frontal or parietal lesions

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HIGHLIGHTS

- Brain areas responsible for attention can be broken down into 3 networks.
- We examined patients with focal brain lesions using the ANT task.
- Patients with frontal lesions showed a deficit in the executive network.
- Patients with parietal lesions showed changes in the orienting network.
- Patients with temporal injuries showed no deficits in any of the 3 networks.

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ABSTRACT

Recently, research on attention has focused on 3 networks that are linked to separate brain regions, i.e. orienting, alerting, and executive control. The attention network test (ANT) is one of the methods to measure the three attention functions. However, neuropsychological investigations have not examined the anatomical disassociation of different attention networks with the same task. We compared the efficiencies of the 3 networks between brain-damaged patients (27 frontal lesions, 20 temporal lesions, and 21 parietal lesions) and healthy controls ($N = 58$) with ANT. Comparing the brain damaged group with the normal controls, a reduced efficiency of the executive network was found in patients with frontal lobe and parietal lobe injuries, and there was also a deficit in the orienting network in patients with parietal lobe injuries. Analysis of lateralization indicated the right hemisphere superiority to the alerting system. The present study found that the three attentional networks were selectively impaired following brain damage which affected different areas in the brain.

1. Introduction

Posner and Petersen [27] proposed that the brain areas responsible for attention were formed by a specific system of anatomical areas, which could be further broken down into 3 networks. These networks carry out functions of alerting, orienting, and executive control [19].

The attentional component of alerting involves the ability to maintain the alert state tonically and the phasic response to a warning signal [18]. The alerting system may relate with some frontal and parietal areas, particularly of the right hemisphere. These regions are activated by continuous alert signals [13]. The alerting system involves cortical projections of the norepinephrine system [17].

The orienting network involves the selection of information among numerous sensory inputs [19]. The research implies that the superior parietal lobe of humans is involved in orienting function of attention [1]. In some fMRI studies orienting task activates areas of the parietal and frontal lobes as well as the temporal–parietal junction, with a right hemisphere bias [10,12]. Substantial empirical evidence emphasizes a role for the parietal cortex in spatial cognition [31]. Evidence from lesion studies confirms the finding of multiple-space representations in the parietal cortex [23]. Blocking cholinergic input to the superior parietal lobe affects the ability to shift attention to cues [15].

Executive control of attention is most frequently measured by instructing a subject to respond to one aspect of a stimulus while ignoring a more dominant aspect [19]. Several studies have reported that executive function deficits are associated with frontal lobe damage, including frontal tumors [22], head injury [14], and frontotemporal dementia. The right inferior frontal gyrus (IFG) plays a role in inhibitory processes relevant for successful executive function, confirmed in the Stroop, Go/No Go, and other

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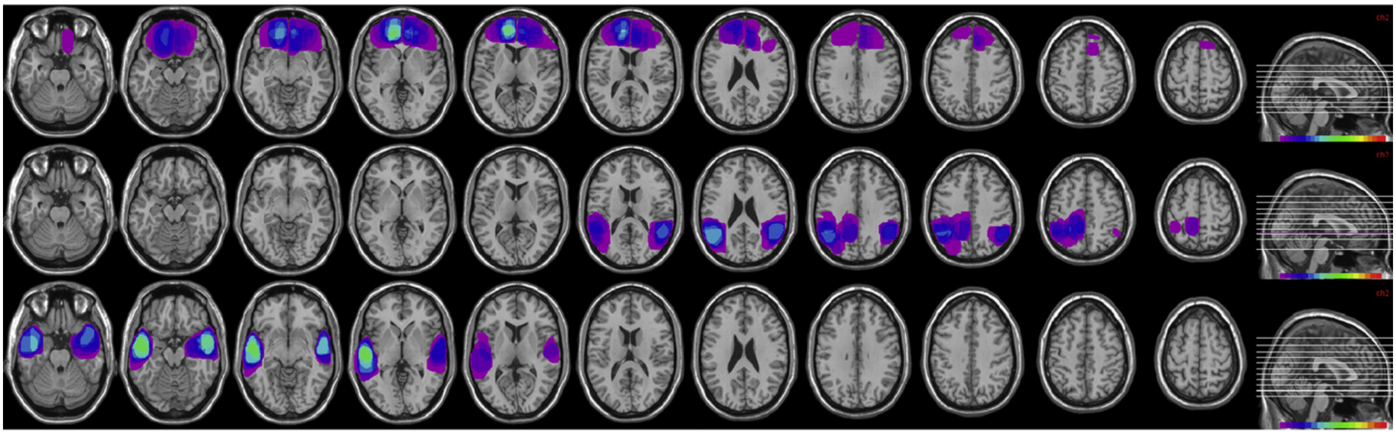

Fig. 1. Lesion location and overlap for patients with left- and right-sided brain injury: frontal lobe (*N* = 27), temporal lobe (*N* = 20), or parietal lobe (*N* = 21).

attention-demanding tasks [2,25,30]. Executive control of attention has been associated with the midline frontal areas (anterior cingulate cortex, ACC) and lateral prefrontal cortex [8], which are target areas of the ventral tegmental dopamine system [26]. Fan and partners have shown that the conflict network is highly heritable [20]. Performance in resolving conflict observed in the ANT relates to two dopamine genes [21].

The attention network test (ANT) provides a measure of the efficiency of the alerting, orienting, and executive attention networks [19]. The unique activation and time courses of the 3 attention networks have also been demonstrated in recent cognitive neuroscience studies [16,18,32]. There is substantial functional overlap among the 3 attentional networks [18,28]. Thus, the focal brain-damaged groups were involved in this study to verify the probable anatomical separability of the three attention networks using the ANT task.

Finally, to minimize the potential confound of brain damage, we took the temporal lobe lesion group into account as brain damaged controls for this domain was not involved in any of the 3 networks.

2. Methods

2.1. Participants

Sixty-eight patients with focal brain lesions confirmed by two neurologist diagnosis were recruited from the First Hospital of Anhui Medical University, between February 2006 and April 2011. The sites of the lesions were documented by means of CT or MRI scans using the lesion overlap technique by MRIcro [6,29] (see Fig. 1).

Inclusion criteria were as follows: (1) the presence of a focal lesion confined to the frontal lobe (FL), temporal lobe (TL), or parietal lobe (PL) with a disease course ranging from 2 months to 24 months; (2) a physical condition that allows participation in the ANT task; (3) absence of childhood-onset epilepsy (late-onset seizures arising from the lesion were allowed); (4) absence of severe aphasia; (5) absence of neglect or hemianopsia; and (6) absence of other significant neurological and psychiatric disorders.

All patients who were admitted to the hospital during the recruitment period, met the inclusion criteria, and consented to participate in the study were included. Patients with tumors were examined post-surgically after a period long enough to avoid the presence of a “mass effect.” The mini-mental state examination (MMSE) was used to measure general cognitive function; Self-Rating Depression Scale was used to exclude depression. Patients were not on anticonvulsant medications at the time of testing.

Fifty-eight age-, sex-, and intellectual level-matched healthy controls (HC) without a history of neurological or psychiatric disorders were recruited and compensated for their participation. Patients and healthy controls were all right-handed. The details are presented in Table 1.

The study was approved by the Ethical Committee of Anhui Medical University (Hefei, PR China). Written informed consent was obtained from all participants.

Table 1
Demographic information, clinical data, and neuropsychological background test scores of patients with brain lesions and healthy controls (HC).

Characteristic	FL lesion patients	PL lesion patients	TL lesion patients	HC
Number of participants	27	21	20	58
Age at testing, years (mean ± SD)	35.6 ± 12.5	37.6 ± 18.1	38.6 ± 16.9	36.3 ± 13.9
Range	(15–55)	(11–62)	(17–68)	(18–67)
Gender (F/M)	17/10	12/9	13/7	34/24
Education level (years)	9.2 ± 2.9	6.7 ± 4.6	8.4 ± 3.8	8.4 ± 3.4
Range	(0–15)	(0–18)	(0–17)	(0–15)
MMSE, mean ± SD	28.6 ± 1.5	27.5 ± 1.9	28.1 ± 1.6	28.9 ± 1.2
Self-Rating Depression Scale, mean ± SD	32.5 ± 5.0	31.6 ± 4.7	30.9 ± 4.0	30.6 ± 4.2
Lesion volume, mean ± SD (cm^3)[a]	17.7 ± 11.2	10.3 ± 4.4	11.1 ± 5.7	–
Range	(3–50)	(3–18)	(1–20)	
Interval between lesion occurrence and neuropsychological evaluation (days)	179	162	145	–
Range	(39–467)	(28–490)	(20–560)	
Etiologies: tumor removal/hematoma or infarction/arteriovenous malformation/abscess or kystis	12/9/4/2	10/7/2/2	9/7/1/3	–
Left lateral/right lateral	14/13	6/15	9/11	–

[a] Lesion volume is equal to long multiplied by the width multiplied by the number of layers, according to the maximum level of lesions in the CT/MRI scan.

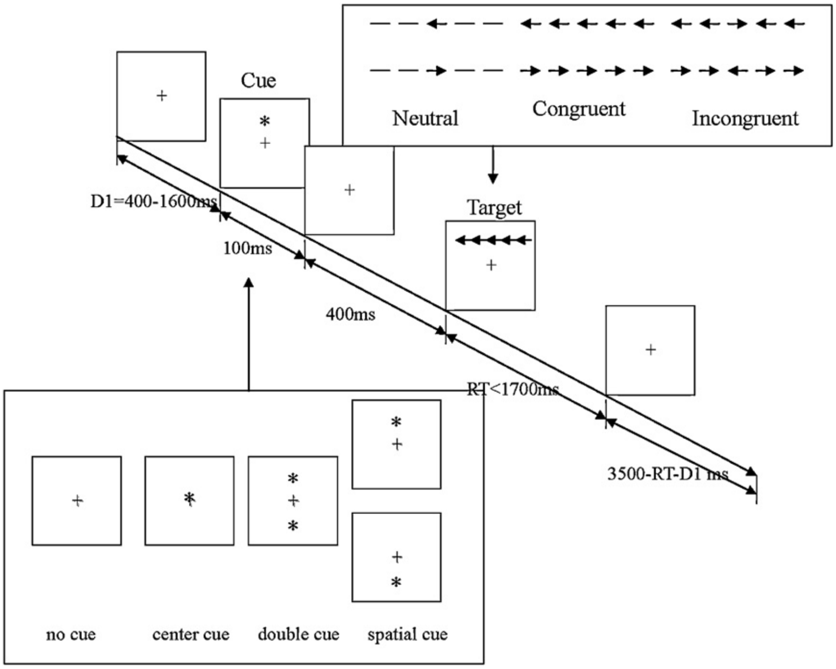

Fig. 2. Schematic of attention network test.

2.2. Attentional network test

We used the ANT as described by Fan et al. in 2002 [19]. All stimuli were displayed on a computer screen. Subjects were instructed to respond via 2 response buttons which requires participants to determine whether a central arrow points left or right. The arrow appears above or below fixation and may or may not be accompanied by flankers. Efficiency of the three attentional networks is assessed by measuring how much response times are influenced by alerting cues, spatial cues, and flankers: alerting effect = $RT_{\text{no cue}} - RT_{\text{center cue}}$, the bigger the difference is, the higher the efficiency of the alerting network would be; orienting effect = $RT_{\text{center cue}} - RT_{\text{spatial cue}}$, the bigger the difference is, the higher efficiency of orienting network would be; conflict effect = $RT_{\text{incongruent}} - RT_{\text{congruent}}$, the bigger the difference is, the lower efficiency of conflicting network would be.

Fig. 2 shows experimental procedure and the four cue conditions and the six target stimuli.

2.3. Statistical analysis

We used SPSS 13.0 software to perform all analyses, and the level of significance was set at $P < 0.05$ for two-tailed tests. Due to the overall parameters do not accord with the normal distribution, group differences were examined using nonparametric test for 2-independent sample (Mann–Whitney *U*-test).

3. Results

3.1. Demographic and clinical data

The means and standard deviations of the demographic and clinical characteristics of patients with brain injury and healthy controls are summarized in Table 1. There were no significant differences in age, gender, educational level, or MMSE among the 4 groups (Table 1).

3.2. Efficiencies of the 3 networks

The mean score and standard error (SE) for each of the attentional networks, mean reaction time (RT) and global accuracy are summarized in Table 2. Compared to the control group, the 3 brain injury groups (FL, PL, TL) had longer overall reaction times (FL, PL, TL: $Z = -1.879, -2.364, -2.392$; $P = 0.060, 0.018, 0.017$ respectively), but similar accuracies (FL, TL: $Z = -1.616$, $P = 0.106$; $Z = -1.636$, $P = 0.102$) except parietal lesion group (PL: $Z = -2.711$, $P = 0.007$). Patients with frontal lobe injuries showed less efficient executive attention than controls ($Z = -3.583$, $P = 0.000$). There were no

Table 2
Attention network scores of patients with brain lesions and healthy controls.

	FL lesion patients	PL lesion patients	TL lesion patients	HC
	Mean RTs (ms) and standard errors			
Alerting	32.6 (5.6)	37.0 (7.4)	30.3 (4.2)	32.6 (2.4)
Ratio	0.042 (0.037)	0.050 (0.046)	0.041 (0.026)	0.048 (0.028)
Orienting	62.8 (5.8)	37.1 (5.8)[b]	56.2 (6.7)	50.9 (2.9)
Ratio	0.086 (0.043)	0.049 (0.035)[a,b]	0.076 (0.042)	0.074 (0.031)
Executive	140.6 (9.2)[a,b]	156.7 (17.8)[a]	116.7 (20.1)	101.3 (4.9)
Ratio	0.183 (0.046)[a,b]	0.193 (0.090)	0.152 (0.101)	0.148 (0.052)
Mean RT	763.3 (26.9)[a]	794.5 (36.6)[a]	779.1 (34.0)[a]	694.0 (13.5)
Accuracy (%)	96.7 (0.6)	95.2 (1.0)[a]	95.3 (1.7)	97.8 (0.3)

[a] Compare to healthy controls.
[b] Compare to temporal lesion group.

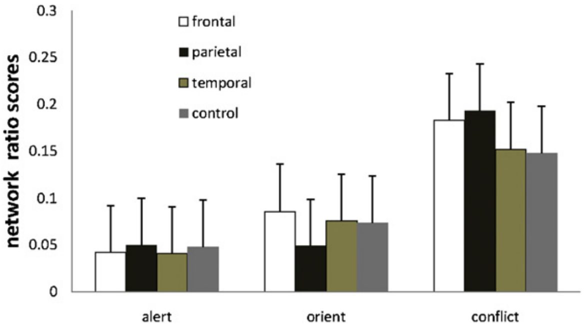

Fig. 3. Network ratio scores for patients and control groups.

statistics differences in the orienting network ($Z = -1.837$, $P = 0.066$) or the alerting network ($Z = -0.595$, $P = 0.552$) compared to normal controls. Further, the executive network efficiency was lower in patients with parietal lobe injuries than in normal controls ($Z = -2.292$, $P = 0.022$). The differences between groups for alerting and orienting scores were not significant ($Z = -0.311$, $P = 0.756$; $Z = -1.877$, $P = 0.061$ respectively), although the data showed a trend reduced orienting scores for parietal lesion patients in comparison with controls. Finally, patients with temporal lobe injuries showed no deficits in any of the 3 networks (alerting, orienting, executive: $Z = -0.498$, -1.214, -0.057; $P = 0.618$, 0.225, 0.954 respectively).

Since response times (RTs) are generally longer in patients with brain injuries, the ratio can be used to examine specific effects that are not influenced by overall reaction time. For each participant, the median RT in each condition was divided by the participant's overall RT. Table 2 shows the ratio scores. Network ratio scores for patients and control groups are also presented in Fig. 3. On the basis of these ratio scores, patients with frontal lobe injuries were significantly different with regard to the executive network compared to the controls ($Z = -2.851$, $P = 0.004$). Meanwhile, patients with parietal lobe lesions showed an impairment in the orienting network ($Z = -2.597$, $P = 0.009$). Comparing the 3 brain injury groups and the control groups, no other statistical differences were found among the 3 network efficiencies ($P\text{s} > 0.05$).

Focal temporal lobe lesions were involved as brain damaged controls, the results of comparison with temporal lobe group are also presented in Table 2. As expected, the data showed that frontal lesion patients took longer time to resolve conflict (less efficient executive attention than temporal lesion group) either in RT scores or ratio scores ($Z = -2.325$, -2.281, $P = 0.020$, 0.023 respectively). Further, the orienting network efficiency was lower in patients with parietal lesion than in temporal lesion group either in RT scores or ratio scores ($Z = -2.233$, -2.400, $P = 0.026$, 0.016 respectively). No other statistical differences were found among the 3 network efficiencies ($P\text{s} > 0.05$). These results demonstrated that the frontal lobe and parietal lobe were the main brain regions of the attentional networks.

3.3. Lateralization of the attentional networks

The mean scores and standard errors (SE) for each of the attentional networks for frontal and parietal lesion patients are summarized in Table 3. In the frontal lesion group, the difference between the left and right brain damage groups for executive network scores was significant ($Z = -1.968$, $P = 0.048$). The differences between groups for alerting and orienting network scores were not significant ($Z = -0.267$, -0.536, $P = 0.793$, 0.616 respectively). In the parietal lesion group, the difference between the left and right brain damage groups for alerting network scores was significant ($Z = -2.072$, $P = 0.036$). The differences between groups for orienting and executive network scores were not significant ($Z = -0.665$, -0.351, $P = 0.519$, 0.733 respectively). Furthermore, the alerting mean score of the right parietal lesion group was lower than normal group (26.2 ± 7.5 ms, 32.6 ± 2.4 ms), but not for the left parietal lesion group (64.2 ± 13.0 ms), which supported the right hemisphere superiority to the alerting system.

4. Discussion

We examined the role of three major brain areas in a series of attentional functions using ANT. The three patient groups showed longer overall reaction time and less accuracy. This might be due to the clumsy movement of limbs. Thus the ratio should be necessary used to examine specific effects that are not influenced by overall reaction time.

One of the main findings of the study is that patients with frontal lesions showed a significant longer RT and higher ratio score benefits for conflicting informative cues compared to the controls. The executive control network consists of the midline frontal areas (anterior cingulate cortex) and lateral prefrontal cortex [5]. The prefrontal cortex is associated with planning complex cognitive behaviors, such as executive function and expression of appropriate social behavior [2]. The present study revealed that patients with frontal lobe injuries had a significant deficit in the executive network and the difference between the left and right brain damage groups for executive network scores was significant. This result indicated that there might be different contributions to the executive attention network. Further, the neocortical dopamine system arising from the ventral tegmental area projects is primarily to the frontal cortex. This projection system is believed to be involved in higher processes related to the control of executive function [7].

Another interesting result of the study is that the executive network efficiency was lower in patients with parietal lobe injuries than that in normal controls but not significant in the ratio scores. Traditionally, frontal lobe functions were related to central executive processes (for a review see [9]). Neuroimaging studies using ANT found no activation of parietal or temporo-parietal junction in the executive control network contrast. One of the possible reasons is that executive function not only relies on prefrontal cortical activation but on a distributed fronto-parietal network

Table 3
Comparison of attention network scores of left and right brain damage patients.

	FL lesion patients (ms)		PL lesion patients (ms)	
	Left side ($M \pm$ SE)	Right side ($M \pm$ SE)	Left side ($M \pm$ SE)	Right side ($M \pm$ SE)
Number	14	13	6	15
Alerting	34.1 (7.0)	31.0 (9.2)	64.2 (13.0)*	26.2 (7.5)*
Orienting	60.5 (7.6)	65.3 (9.1)	29.8 (12.6)	40.1 (6.5)
Executive	127.2 (12.5)*	155 (13.0)*	144.0 (35.9)	161.7 (21.0)
Mean RT	731.0 (32.4)	798.2 (42.9)	734.0 (35.9)	818.7 (48.4)
Accuracy (%)	96.4 (0.6)	96.9 (1.1)	96.7 (1.1)	94.7 (1.3)

* $P < 0.05$.

[4,24]. The frontal network for executive attention which needs an intact parietal lobe in order to function optimally. Another possible reason is that the conflict effect of the executive control network was calculated by subtracting the mean RTs of the conditions with congruent flankers from the mean RTs of the conditions with incongruent flankers. Impairment in only the orienting network made focusing the attention on the location of stimulus so hard that the reaction times in both congruent and incongruent conditions were disproportionally increased. In this situation execution function seems impaired although the execution network is intact.

The parietal lobe is known to be involved in spatial processes. The present study demonstrated that the efficiency of the orienting network was significantly lower in patients with parietal lobe injuries than that in normal controls in ratio scores. Neuroimaging studies shows that orienting task activates areas of the parietal and frontal lobes as well as the temporal–parietal junction [18]. In the parietal lesion group, the differences between the left and right brain damage groups for orienting and executive network scores were not significant, although the data showed a trend reduced orienting scores for left and right parietal injury patients in comparison with controls. Attentional orienting is traditionally lateralized to the right hemisphere. However, neuroimaging studies reported divergent results. An overlap activation was found in a large fronto-parietal area network, including bilateral premotor cortex, bilateral posterior parietal cortex and medial frontal cortex [11]. Meanwhile, the difference between patients with frontal lobe injuries and normal controls showed no deficit in the orienting attention network. Furthermore, in the analysis of lateralization of the attentional networks in the frontal lesion group, there were no significant differences for orienting and alerting network scores, which indicated that there might be similar contributions of the left or right frontal lobe to the two networks.

Alerting is an important source of attention that maintains an adequate level of alertness, and it is critical for optimal performance. Imaging studies investigating brain regions involved in the control of alerting have demonstrated that there is an activation of thalamic, frontal, and parietal areas, particularly of the right hemisphere [3,27]. The results of the present study showed that the alerting mean score of the right parietal lesion group was lower than normal group, nor was the left parietal lesion group, which supported the right hemisphere superiority to the alerting system. This result is similar to the sustained attention condition in prior studies where there was strong evidence for right parietal activation [27].

Finally, we took the temporal lobe lesion group into account as brain damaged controls to minimize the potential confound of brain damage. As expected, patients with temporal injuries showed no deficit in any of the 3 networks. Comparing to temporal lobe group, frontal and parietal lesion groups showed less efficient executive attention and orienting network respectively, either in RT scores or in ratio scores.

In conclusion, the findings obtained confirm previous reports, suggesting that alerting, orienting and executive attention might be mediated by different neural mechanisms. It is necessary to consider localizing the attention networks in more specific areas.

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