

The activation of attentional networks

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Received 26 July 2004; revised 27 January 2005; accepted 4 February 2005
Available online 19 March 2005

Alerting, orienting, and executive control are widely thought to be relatively independent aspects of attention that are linked to separable brain regions. However, neuroimaging studies have yet to examine evidence for the anatomical separability of these three aspects of attention in the same subjects performing the same task. The attention network test (ANT) examines the effects of cues and targets within a single reaction time task to provide a means of exploring the efficiency of the alerting, orienting, and executive control networks involved in attention. It also provides an opportunity to examine the brain activity of these three networks as they operate in a single integrated task. We used event-related functional magnetic resonance imaging (fMRI) to explore the brain areas involved in the three attention systems targeted by the ANT. The alerting contrast showed strong thalamic involvement and activation of anterior and posterior cortical sites. As expected, the orienting contrast activated parietal sites and frontal eye fields. The executive control network contrast showed activation of the anterior cingulate along with several other brain areas. With some exceptions, activation patterns of these three networks within this single task are consistent with previous fMRI studies that have been studied in separate tasks. Overall, the fMRI results suggest that the functional contrasts within this single task differentially activate three separable anatomical networks related to the components of attention.

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Keywords: Attention; Attentional networks; Alerting; Orienting; Executive control; fMRI

Introduction

The study of attention has been important for the integration of cognitive approaches with neuroscience (Desimone and Duncan, 1995; Kastner and Ungerleider, 2000; Miller and Cohen, 2001;

Posner, 2004; Posner and Petersen, 1990). There is widespread agreement from imaging (Corbetta et al., 2000; Kastner et al., 1999) and cellular recording studies (Desimone and Duncan, 1995) that orienting to sensory information activates a common network of neural areas even before a target is presented. This suggests that there is a specific network that serves as the source of the enhancement of neural signals related to processing a target. Similarly, neuroimaging studies have revealed a specific network of areas that relate to obtaining the alert state (Coull et al., 1996; Pardo et al., 1991; Posner and Petersen, 1990) and to resolving conflict among responses (Botvinick et al., 1999; MacDonald et al., 2000). However, each of these forms of evidence comes from separate experiments each with unique task demands, which precludes direct examination of the separability of these networks within the same task.

We developed an attention network test (ANT) to provide a behavioral measure of the efficiency of the three attentional networks within a single task (Fan et al., 2002). The ANT is designed to provide an overall assay with the minimum number of trials. It does not use a validity manipulation of cues. However, the ANT provides outcome measures that indicate the efficiency of the networks that perform the alerting, orienting, and executive (conflict resolution) functions of attention. Since our original report, the ANT has been widely used as a behavioral test to assay performance of normal children (Mezzacappa, 2004; Rueda et al., 2004) and those with disorders (Bish et al., 2005; Sobin et al., 2004), adults with borderline personality disorder compared to temperamentally matched controls (Klein, 2003; Posner et al., 2002), and patients with schizophrenia (Wang et al., in press) and with Alzheimer's disease (Fernandez-Duque and Black, in press). Other studies of autism, attention deficit disorder, mild traumatic brain injury, and the effects of training are also in progress.

In addition, we have shown that the conflict network is highly heritable (Fan et al., 2001). Performance in resolving conflict using the ANT relates to two dopamine genes (Fossella et al., 2002). Although exactly how and where these genes influence dopamine release is not clear, alleles of the DRD4 and MAOA

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Available online on ScienceDirect (www.sciencedirect.com).

gene did show differential activation of the anterior cingulate in a study using fMRI (Fan et al., 2003b). Interestingly, MAOA alleles that are predicted to result in higher levels of extra-synaptic dopamine did not show associations with more efficient cognition, but rather were associated with less efficient executive attention performance. These results stand in contrast with other studies that combine imaging and genetics to explore individual differences where alleles that predict higher levels of DA were associated with more efficient executive function (Egan et al., 2001; Mattay et al., 2003).

In our original report of work with the ANT (Fan et al., 2002), we found there was a good deal of support for independence between networks. This was shown by the lack of correlation between the scores obtained for each network and the existence of only two small interactions in which the no cue and spatial cue conditions both reduced the degree of conflict. In a larger sample study using the ANT (Fossella et al., 2002), we have found a small but significant negative correlation between the alerting and conflict scores. Moreover, with specific changes to the paradigm, additional interactions between the network scores have been observed. For example, in a study using a tone for the alerting signal and manipulating validity of the visual cue, it was found that the alerting network inhibits the executive network and the orienting network enhances the executive network (Callejas et al., 2004). Although the original configuration of the ANT demonstrated independence of the networks, it would be surprising if the networks did not communicate and thus influence each other with other task demands. Although previous imaging studies suggest that the networks of neural areas serving as the sources of the orienting, alerting, and conflict effects are anatomically separable, there is substantial functional overlap. The most extensive data are on an orienting network that includes the superior parietal lobe, temporal parietal junction, and frontal eye field (Corbetta and Shulman, 2002). Sometimes these effects have been thought to be due to a shift of the focus of attention to the target location and they have also sometimes been thought of as a change of focal length to incorporate a larger area. By comparing a peripheral cue with a small central cue we attempt to encourage a shift of attention to the new location. In support of this idea, we found the spatial cue condition to reduce the flanker effect as though a smaller focus of attention is obtained when the person is specifically cued to the center arrow (Fan et al., 2002).

There are data relating the norepinephrine network to alerting that include thalamic, frontal, and parietal areas (Coull et al., 1996; Marrocco and Davidson, 1998; Posner and Petersen, 1990). Imaging studies of the executive network involved in the control of conflict have consistently activated areas of the dorsal anterior cingulate and often the lateral prefrontal cortex (Bush et al., 2000; MacDonald et al., 2000). However, these results were obtained in separate studies, with methods that differ from those of the ANT, therefore the extent of anatomical separation is not known. It is important to see the extent to which these previous imaging results apply to the ANT, where the three networks are activated in a single study designed to maximize their functional independence in order to determine separation and overlap in the functional anatomy of the three networks.

The present study attempted to isolate the neural networks responsible for performance on the three indices of the ANT. To most directly test the separability of these three networks, we took advantage of the unique design of the ANT to measure these effects within the same group of subjects during performance of the

same blocks of scanning. We ran an event-related fMRI experiment using the ANT to find brain areas active for the three attentional networks. We hypothesized that a pattern of separable activity would emerge with specific attentional functions loading heavily on segregated anatomical areas. We explored the following specific hypotheses based on previous studies that have isolated each network within separate tasks on separate subjects: (1) alerting would activate the frontal and parietal areas of the right and/or left hemisphere and thalamic areas that are potentially related to norepinephrine (Coull et al., 2000, 2001; Marrocco and Davidson, 1998). Early neuroimaging and lesion studies together with evidence of a right hemisphere bias in NE have suggested a right hemisphere basis for sustained attention (see Posner and Petersen, 1990 for a summary). However, more recent fMRI studies have suggested that cues calling attention to a temporal interval might activate left hemisphere areas (Coull et al., 2000, 2001); (2) orienting would activate a superior parietal region and the temporal parietal junction, with a right hemisphere bias (Corbetta et al., 2000); and (3) conflict would activate anterior cingulate cortex (ACC) and a left lateral frontal bias might be suggested for the importance of dopamine for this system (Bush et al., 2000; MacDonald et al., 2000).

Methods

Subjects

Sixteen right-handed normal adults (mean age = 27.2 years, SD = 5.7 years, range: 18–36 years; 8 female) participated in this study. They were scanned in a scanner while they carried out the ANT. A signed informed consent approved by the New York Presbyterian Hospital/Weill Medical College of Cornell University was obtained from each participant prior to the experiment.

Attentional network test (ANT)

A version of the ANT was adapted to optimize the attentional contrasts for the fMRI study. We used three cue conditions (no cue, center cue, spatial cue) and two target conditions (congruent and incongruent). These conditions were selected from a large set of conditions tested in the original behavioral study (Fan et al., 2002) in which there were four cue conditions (no cue, center cue, double cue, and spatial cue) and three target conditions (congruent, incongruent, and neutral). The details of this simplified version of the ANT are illustrated in Fig. 1. Stimuli consisted of a row of 5 visually presented horizontal black lines, with arrowheads pointing leftward or rightward, against a gray background. A single arrow subtended 0.58° of visual angle and the contours of adjacent arrows or lines were separated by 0.06° of visual angle. The stimuli (one central arrow plus four flankers) subtended a total 3.27° of visual angle. The target was a leftward or rightward arrowhead at the center. To introduce a conflict resolution component, the central arrow was “flanked” by congruent or incongruent stimuli. The target was flanked on either side by two arrows in the same direction (congruent condition) or in the opposite direction (incongruent condition). The participants’ task was to identify the direction of the centrally presented arrow by pressing a button with the index finger of the left hand for the left direction and a button with the index finger of the right hand for the right direction.

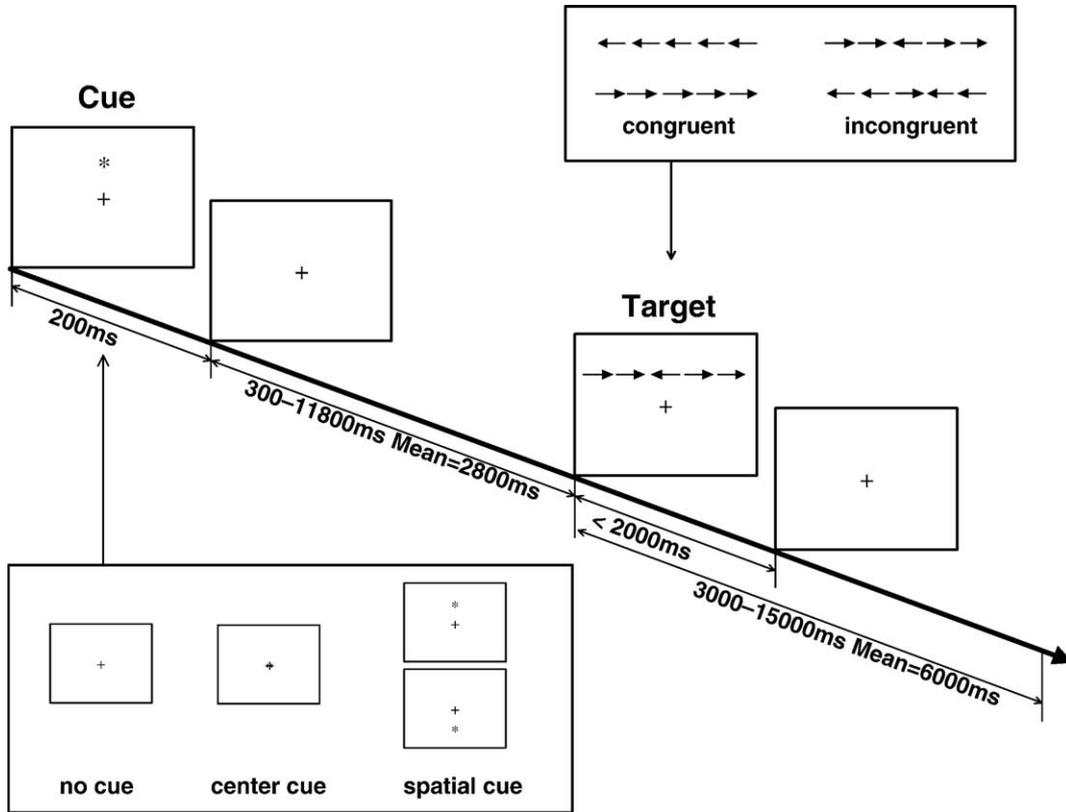


Fig. 1. Schematic of attention network test. In each trial, a fixation cross appears in the center of the screen all the time. Depending on the cue condition, a cue (none, center, or spatial cue) appears for 200 ms. After a variable duration (300–11 800 ms), the target (the center arrow) and flankers of left and right two arrows (congruent or incongruent flankers) are presented until the participant responds with a button press, but for no longer than 2000 ms. After the participant makes a response, the target and flankers disappear immediately and a post-target fixation period lasts for a variable duration (from the onset of the target and the start time of the next trial is between 3000 and 15 000 ms).

To introduce an attentional orienting component to the task, the row of 5 arrows was presented 1.06° above or below the fixation point in the center of the screen. Thus the subject had to shift spatial attention from the fixation point to the target stimulus on each trial in order to determine the proper response. To measure the alerting or/and orienting benefits, there were three warning conditions: no-cue (baseline), center-cue (alerting, temporally informative), and spatial-cue (alerting plus orienting, temporally, and spatially informative). Comparing the performance of one condition to an appropriate reference condition, the operational definitions of the efficiencies of the three attentional networks for the behavioral analysis were defined so as to produce in each case a positive score:

$$\text{Alerting effect} = RT_{\text{no cue}} - RT_{\text{center cue}}$$

$$\text{Orienting effect} = RT_{\text{center cue}} - RT_{\text{spatial cue}}$$

$$\text{Conflict effect} = RT_{\text{incongruent}} - RT_{\text{congruent}}$$

We used event-related fMRI to study the activations of these attentional networks. In order to separate brain activity to the cues and targets, we jittered the time intervals between cue and target and between the target and the next trial. A fixation cross appeared at the center of the screen during the whole trial. In each trial, depending on the condition, either a cue (asterisk) was presented for 200 ms or the fixation remained unchanged (the no cue condition). After a variable duration (one of a set of 12 discrete

times from 300 to 11 800 ms, including three 300-ms intervals, as well as 550, 800, 1050, 1550, 2300, 3300, 4800, 6550, and 11 800 ms, approximating an exponential distribution with a mean interval of 2800 ms), the target and flankers were presented until the participant responded or 2000 ms elapsed. The duration between the onset of the target and the start time of the next trial was also varied systematically (a set of 12 discrete times from 3000 to 15 000 ms, including 3000, 3250, 3500, 3750, 4000, 4500, 5000, 5500, 6500, 8000, 10 000, and 15 000 ms, approximating an exponential distribution with a mean of 6000 ms).

There were six runs in this experiment with 36 test trials plus two buffer trials in each. In each run, the six trial types (3 cue conditions by 2 target conditions) were presented in a predetermined counterbalanced order to ensure that each trial type followed every other trial type equally often. The order was also counterbalanced by rotating the six trial types across the six runs. Since 12 intervals did not lend themselves to counterbalancing with 36 trials, for every 12 trials of the 36 trials per run, the 12 intervals between cue and target and the 12 intervals between target and next trial were randomized until the Spearman's rank correlation between interval pairs was less than 0.005. The two buffer trials were the same as the last two trials of the 36 test trials with mean cue to target interval and mean target to next trial interval.

We isolated brain activity associated with alerting by subtracting a no cue condition from a center cue condition. The idea was that both the no cue and center cue required sustained attention, but the center cue also provided information on when the target would

occur, allowing subjects to enter a more alert state. This is the opposite subtraction from the behavioral data. Brain activity associated with orienting was determined by subtracting the center cue condition from the spatial cue condition. The spatial cue was thought to add to the central cue an orienting operation prior to the occurrence of the target. Note that in the behavioral experiment the benefit of orienting was obtained by subtracting the spatial cue response from the slower center cue response. In the imaging experiment, however, the opposite subtraction was performed to isolate regions more active in response to the spatial cue. Finally, the same incongruent minus congruent subtraction was used to isolate the executive network in both the behavioral and fMRI data analysis.

Acquisition of anatomical and functional MRI data

MR imaging was carried out using a 3-T GE Signa scanner. Functional scans were collected by using a T2*-weighted gradient echo planar imaging (EPI) sequence (TE = 35 ms, TR = 2000 ms, flip angle = 80°) with an in-plane resolution of $3.44 \times 3.44 \text{ mm}^2$ (64×64 matrix; $220 \times 220 \text{ mm}^2$ field of view). To cover the whole brain, twenty-four 5-mm slices (skip 1 mm between slices) were acquired along the AC–PC plane as determined by the midsagittal section. Structural scans were collected using a T1-weighted sequence in the same orientation as the functional sequences to provide detailed anatomic images aligned to the functional scans. A high-resolution structural MRI sequence (FOV = $220 \times 220 \text{ mm}^2$, 256×256 matrix, thickness = 1.5 mm, slice number = 100) was acquired for the purpose of normalization. Distortion in EPI images was corrected based on the estimated parameters of the phase map (Jezzard and Balaban, 1995).

Analysis of functional MRI data

Image preprocessing and statistical analysis were conducted using SPM99 (Statistical Parametric Mapping, Wellcome Department of Imaging Neuroscience, Institute of Neurology, London, UK). EPI time-series images were reconstructed and preprocessed off-line to be ready for the statistical parametric mapping. A timing correction procedure was used to correct differences in image acquisition time between slices by shifting forward the time series data on each slice using sinc-interpolation. The spatial alignment was performed to realign the time-series of images acquired from the same subject to the first volume using a least squares approach and a six-parameter (rigid body) spatial transformation. EPI images were registered to each participant's T1 structural images and then to the high-resolution images. The high-resolution images were normalized to a standard template from the Montreal Neurological Institute (MNI). Then the transformation parameters were applied to the EPI images. After normalization, voxels were resampled with a $2 \times 2 \times 2 \text{ mm}^3$ voxel size. An $8 \times 8 \times 12 \text{ mm}$ full-width-at-half-maximum (FWHM) Gaussian kernel was used to smooth the EPI images.

High-pass filtering was applied to the time series of EPI images to remove the low-frequency drift in EPI signal. The global change in signal intensity was removed by proportional scaling. Then statistical analysis, which was based upon general linear modeling (GLM), was conducted. The data from each participant were analyzed by using linear regression between the observed event-related EPI signals and regressors to identify patterns of activation.

Regressors were created by convolving a train of delta functions that represent the individual trial events (fixation with no cue, central cue, spatial cue, targets with congruent flankers, targets with incongruent flankers) with the base functions and its derivative. The base functions were a synthetic hemodynamic response function composed of two gamma functions (Friston et al., 1998). Each of the regressors represents one expected brain response to the event. The linear combination of all of the regressors was used for the modeling of the response of the brain to the experimental conditions or events. Six realignment parameters were used as covariates.

Group data analysis was then conducted. A random-effects analysis, called the second level data analysis, was carried out to make inferences to the population. The contrast images (center cue-no cue for alerting, spatial cue-center cue for orienting, and incongruent flanker-congruent flanker for conflict) from each subject were the input data. To determine whether there was significant activation corresponding to each contrast, the resultant parameter estimates for each contrast at each voxel were tested using a *t* test. An uncorrected *P* value 0.05 for the height (intensity) threshold of each activated voxel was used. A Monte Carlo simulation of the brain volume of current study was conducted to establish an appropriate voxel contiguity threshold (Slotnick et al., 2003). Assuming an individual voxel type I error of $P < 0.05$, a cluster extent of 9 contiguous original voxels ($3.4375 \times 3.4375 \times 6 \text{ mm}^3$) was indicated as necessary to correct for multiple voxel comparisons at $P < 0.05$. Converted to the resampled voxel ($2 \times 2 \times 2 \text{ mm}^3$), the threshold for cluster extent was 80 voxels. The coordinates in MNI space were transferred to Talairach space (Talairach and Tournoux, 1988) using a non-linear transform (<http://www.mrc-cbu.cam.ac.uk/Imaging/mnispace.html>).

We examined all of the areas in which there was evidence of a conjunction between activations of alerting and orienting, alerting and conflict, and orienting and conflict. A common activation criterion was defined such that a region must show significant activation individually in each of the two networks and show evidence of a significant conjunction activation using a height threshold of $P = 0.05$ and an extent threshold of $k = 80$ voxels, given a voxel size of $2 \times 2 \times 2 \text{ mm}^3$.

Results

Behavioral results

Table 1 shows the mean RTs for each condition of the ANT performed during the scan. Repeated measures ANOVA of RT showed that the main effect of target condition (conflict effect) was

Table 1
Mean RT (and SD) and accuracy (and SD) for each condition

	No cue	Center cue	Spatial cue	Mean
Congruent				
RT	773 (132)	699 (106)	679 (103)	717 (110)
Accuracy	0.95 (0.08)	0.95 (0.08)	0.96 (0.09)	0.95 (0.08)
Incongruent				
RT	863 (137)	817 (126)	775 (143)	818 (132)
Accuracy	0.92 (0.11)	0.94 (0.08)	0.92 (0.11)	0.93 (0.09)
Mean				
RT	819 (131)	758 (110)	727 (119)	768 (118)
Accuracy	0.93 (0.09)	0.95 (0.09)	0.96 (0.09)	0.94 (0.08)

significant, $F(1,15) = 50.86$, $P < 0.01$. The main effect of cue condition was significant, $F(2,30) = 30.81$, $P < 0.01$. The interaction between target condition and cue condition was not significant, $F(2,30) = 1.51$, ns. The alerting effect was significant, $F(1,15) = 49.83$, $P < 0.01$, and the orienting effect was significant, $F(1,15) = 12.87$, $P < 0.01$. Table 2 shows the alerting, orienting, and conflict effects and the correlations among them. The mean RT was 768 ms. The three attentional network scores were alerting (60 ms benefit), orienting (31 ms benefit), and conflict (102 ms cost). These three attention network scores were similar to previously published findings (Fan et al., 2002). As in the previous study, there were no significant correlations between the network scores. The ANOVA on accuracy showed that only the conflict effect was significant, $F(1,5) = 7.25$, $P < 0.05$. The cue effect and interaction were not significant, $F(2,30) < 1$ and $F(2,30) = 1.42$ ns. There was no evidence of a speed accuracy tradeoff. Rather, as expected, low accuracy was associated with long RTs. Responses to incongruent stimuli were slower and less accurate than congruent, spatial cues led to fastest and most accurate responses, and no cue conditions were the slowest and least accurate of the three cue conditions.

fMRI results

Alerting

Following the central cue as a warning signal, we found the classic fronto-parietal cortical activation along with the thalamus (see Fig. 2 alerting network). Anterior intraparietal (BA 7) activity, inferior parietal, and frontal activity were stronger within the left vs. the right hemisphere. The superior colliculus (involved in vision) was also activated. The right temporal parietal junction (BA22) showed a significant activation. Other areas activated are also shown in Table 3. We also conducted a correlation analysis to examine whether the slowest subjects were the ones who showed the most left lateralization for the alerting effect. Slower RT was associated with bilateral parietal lobe and insula activation but with more area on right superior parietal lobe (BA7, $x = 27$, $y = -43$, $z = 41$), and right middle frontal gyrus (BA 46, $x = 36$, $y = 34$, $z = 23$). Thus slow RTs were not the cause of the left laterality found for alerting.

Orienting

Activity was found in the left and right superior parietal lobe as expected. The left temporal parietal junction (BA39, $x = -42$, $y = -63$, $z = 16$, peak $Z = 2.08$, voxel number = 53) showed a significant peak value but did not reach the cluster size criterion. Left precentral gyrus which is close to frontal eye field (FEF) (Paus, 1996) showed significant activation. Table 4 and Fig. 2 (orienting network) show the activations associated with orienting.

Executive control

Table 5 shows the activations for the conflict effect. Anterior cingulate plus right and left frontal areas were active as predicted,

but several other areas, for example, left and right fusiform gyrus, were active as well, reflecting the complex nature of the flanker task (see Fig. 2 executive network).

Conjunction analysis

There was no area that met the stringent criterion for conjunction analysis of alerting and orienting. This might be due to the fact that there was no overlap between alerting activation and orienting activation in the two separate subtractions. The conjunction analysis of alerting and conflict showed that the thalamus and left fusiform gyrus (BA 37, $x = -48$, $y = -58$, $z = 0$, peak $Z = 3.58$) share common activations for these two networks. There was no common activation for the conjunction analysis of orienting and conflict activity.

Discussion

Overall, results support the initial hypotheses that specific attention networks operating within the same subjects and within the same task-blocks are associated with separable activation patterns loading on specific anatomical regions. Several studies have suggested that alerting depends upon the norepinephrine system by showing that the effect of warning signals is reduced or eliminated by norepinephrine antagonists (Coull et al., 1996, 2001; Marrocco and Davidson, 1998). We studied alerting by use of a warning signal indicating when, but not where, a stimulus will occur. Patient studies have suggested that lesions of the frontal and parietal lobe, particularly of the right hemisphere, have strong effects on sustained attention and reduce the ability of patients to maintain the alert state in the absence of a warning signal (Posner and Petersen, 1990; Robertson et al., 1995; Sturm and Willmes, 2001). This anatomy was supported by an early PET study requiring the maintenance of vigilance toward a sensory signal for a brief period (Pardo et al., 1991). However, more recent fMRI studies confirm the involvement of parietal and frontal sites in alerting, but extend these findings to show that the specific impact of a warning cue preceding a target by a short interval activates left hemisphere sites (Coull et al., 2000, 2001; Nobre, 2001). Thalamic activation following a warning signal has also been reported (Kinomura et al., 1996).

The activated networks in our study generally fit with those hypothesized from the literature. One finding which might at first seem to be an exception is the strong left hemisphere activity in the frontal and parietal areas in the warning cue minus the no cue subtraction. The no cue condition is one in which subjects have to maintain the alert state from the last trial with no cue as to the correct time interval. This is similar to the sustained attention condition in prior studies where there was strong evidence for right frontal and parietal activation (Posner and Petersen, 1990). In the central cue condition, subjects receive a cue as to when the target will be presented. This is the very condition for which Coull et al. (2001) found primarily left hemisphere activation. Thus, the center cue minus no cue subtraction is likely to show primarily the left frontal activity shown in the center cue condition, but as we see also shows some right parietal activation possibly because of different localization in the spatial and center cue conditions.

In the work of Coull et al. (2001), it was possible to separate the influence of the cue on general alerting from its influence on orienting to a particular time interval indicated by the cue by use of valid and invalid temporal interval cues. This has not been done in the ANT. However, the strong left-sided laterality for alerting as

Table 2
Behavioral effects and correlations

	Effect and SD (ms)	Alerting	Orienting	Conflict
Alerting	60 (34)			
Orienting	31 (34)	0.258		
Conflict	102 (57)	0.258	0.155	
Mean RT	768 (118)	0.556 ^a	-0.180	0.385

^a Correlation is significant at the 0.05 level (2-tailed).

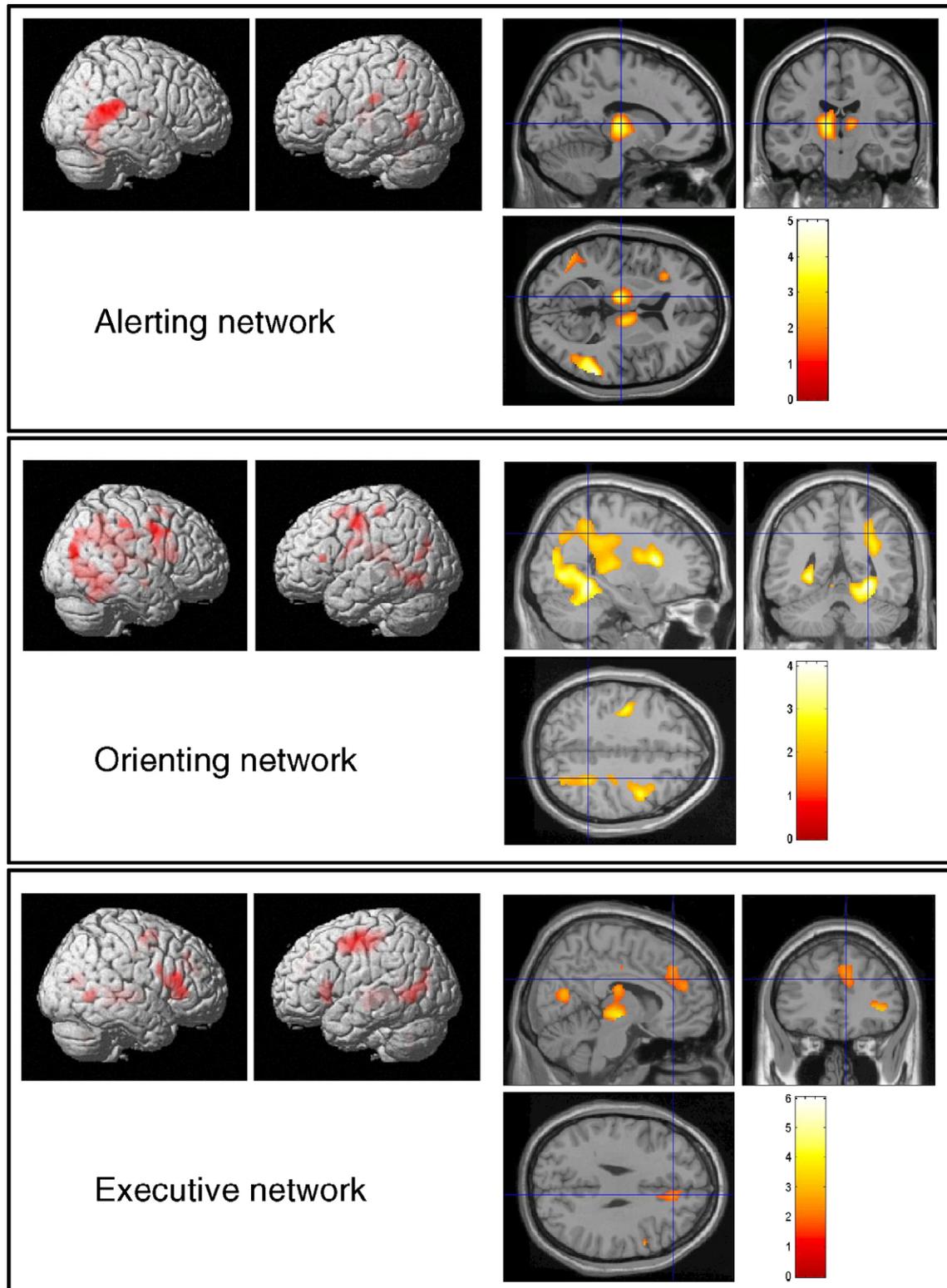


Fig. 2. fMRI results for the three attentional networks. The cross-section view of activations of the alerting network shows the thalamic activations of the alerting effect. The cross-section view of the orienting network shows parietal activation. The cross-section view of the conflict network shows ACC activation.

measured by central cue minus no cue suggests that the cue was used to predict the time of the target and thus served as a temporal orienting cue. This would account for the stronger left hemisphere activation that we found.

There is widespread agreement on the brain areas involved in orienting toward the spatial location of visual signals (Corbetta and Shulman, 2002; Kastner et al., 1999). Typically, activation is indicated in prefrontal areas (frontal eye fields) and parietal areas

Table 3
Regions activated for alerting: center-cue minus no-cue

Region	BA	X	Y	Z	Z score	P ^a	Voxel ^b
R superior temporal gyrus ^c	22	61	-40	11	3.78	0.000	1397
Superior colliculus		6	-28	-7	3.64	0.000	2311 ^d
L thalamus		-12	-17	6	3.17	0.001	
R thalamus		13	-9	7	2.85	0.002	
L inferior parietal lobe	40	-50	-20	21	3.09	0.001	132
L fusiform gyrus	37	-42	-62	0	2.81	0.002	370
L inferior frontal gyrus	47	-32	27	0	2.70	0.003	130
Cerebellar vermis		0	-65	-10	2.49	0.006	100
L superior parietal lobe ^e	7	-36	-46	50	2.43	0.008	168

^a Height threshold: $P < 0.05$, uncorrected.

^b Extent threshold: $k > 80$ voxels, voxel size = $2 \times 2 \times 2$ mm³.

^c Subregion of temporal parietal junction (TPJ).

^d Includes superior colliculus, L and R thalamus.

^e Anterior intraparietal sulcus (AIPS).

including both the superior parietal cortex and temporal parietal junction. Several studies show a right hemisphere bias particularly for shifting attention from a cued position to the position of the target when these differ. Lesion data generally show that deficits in the right parietal lobe, most often at the temporal parietal junction, are most effective in producing neglect of contralateral stimulation (Robertson et al., 1995). The temporal parietal junction activation is most clearly seen when shifting attention following an invalid cue (Corbetta and Shulman, 2002; Thiel et al., 2004). Although most studies use a validity manipulation, the ANT was designed to use completely reliable cues in order to achieve the maximal separability of orienting and executive networks. However, it is likely that both methods are sensitive to cost as well as benefit. In the ANT, valid peripheral cues are subtracted from a condition in which the center cue appears at fixation before the target appears in the periphery. Thus in the center cue condition subjects must disengage from the central location when the target appears, and this represents a cost that is not present in the peripheral cue

Table 4
Regions activated for orienting: spatial-cue minus center-cue

Region	BA	X	Y	Z	Z score	P	Voxel
L fusiform gyrus	37	-34	-60	-5	3.29	0.000	1396
R fusiform gyrus	37	30	-47	-6	3.25	0.001	6637
L precentral gyrus ^a	6	-38	-8	41	2.94	0.002	523
R superior parietal lobe ^b	7	32	-41	30	2.66	0.009	125
L superior frontal gyrus	6	-10	7	57	2.63	0.004	517
L superior parietal lobe ^c	7	-28	-72	28	2.12	0.017	118
R postcentral gyrus	2	57	-21	43	2.10	0.018	83
L precentral gyrus	4	-30	-26	53	1.97	0.025	130

^a Close to frontal eye field (FEF).

^b Anterior intraparietal sulcus (AIPS).

^c Junction of intraparietal and transverse occipital sulcus (IPTO).

Table 5
Regions activated for executive attention: incongruent minus congruent

Region	BA	X	Y	Z	Z score	P	Voxel
Thalamus ^a		-22	-27	3	4.23	0.000	2972
L superior frontal gyrus ^b	6	-16	4	44	3.22	0.001	2516
R inferior frontal gyrus	45	36	26	15	3.13	0.001	908
L fusiform gyrus	37	-36	-60	1	3.09	0.001	1492
L inferior frontal gyrus	47	-34	20	5	2.92	0.002	313
Cerebellar vermis		0	-62	-32	2.47	0.007	128
R middle frontal gyrus	6	36	-5	50	2.39	0.008	307
R fusiform gyrus	37	44	-58	1	2.38	0.009	201
R anterior cingulate gyrus	32	6	36	26	2.20	0.014	398

^a Peaks at left and right pulvinar.

^b Close to frontal eye field (FEF).

condition. However, since no target ever occurs at the central location, the extent of engagement at this location is probably lower than when invalid cues are used. Results of our study demonstrate that this subtraction produces similar results to other orienting findings typically obtained through the use of invalid cues except for activation of the temporal parietal junction.

A number of neuroimaging studies have shown that dorsal ACC is involved in dealing with conflict resolution when a person is required to respond based on one stimulus dimension while ignoring another conflicting dimension (Bush et al., 2000). It has been proposed that ACC function is a domain general process of monitoring conflict while dorsolateral prefrontal cortex is involved in resolving conflict (Botvinick et al., 2001; Carter et al., 1999; MacDonald et al., 2000). Previously, we demonstrated three types of conflict tasks activated similar areas within the anterior cingulate (Fan et al., 2003a). When the task required a person to respond to the direction of a central arrow while ignoring flanking arrows that either pointed in the same (congruent) or the opposite (incongruent) direction, we found that the ACC and left frontal cortex had greater activation for the incongruent condition (Fan et al., 2003a). In this study, the executive network contrast (conflict) produced activation in the anterior cingulate and frontal areas as expected. Importantly, these activations were demonstrated to be separable from activations associated with alerting and orienting functions. However, these results do not indicate that processing differences between the congruent and incongruent trials are specific to these regions. The large number of other areas found active in the subtraction of congruent from incongruent trials suggests the presence of multiple operations, many of which may not be necessarily related to resolving conflict.

The ANT provides three subtractions which we believe relate closely to the networks for alerting, orienting, and executive control. Our current behavioral data collected within the scanner were quite similar to what we had previously obtained from a larger number of subjects ($n = 40$) in a behavioral study run outside the scanner (Fan et al., 2002). The fMRI results of the ANT largely confirm the implication from behavioral data for three separable networks. Each set of cognitive subtractions identified a rather large number of areas. Our analysis suggests that the networks identified by each subtraction are rather distinct, providing

evidence that the relative independence of the three attentional networks may be supported by distinct networks separable within the same task, within the same blocks of test, and within the same subjects.

However, the current results also indicate findings of overlap between attention networks. One such exception is BA 7 which is activated both by alerting and orienting cues, although these effects failed to reach significance in the conjunction analysis. Non-human primate studies suggest that alerting and orienting functions are dissociable at the level of neurotransmitter systems. Studies using alert monkeys with peripheral (exogenous visual cues) show that drugs which influence NA abolish warning signal effects while leaving orienting intact, while drugs that affect Ach influence orienting but not alerting (Davidson and Marrocco, 2000; Marrocco and Davidson, 1998). Perhaps one reason the ANT fails to demonstrate this strong dissociation is related to the use of a 100% valid peripheral cue, which is likely to recruit some form of voluntary control. However, it is not known whether the neurotransmitter results would be different when strictly voluntary control is involved, as in the case of a central symbolic cue (e.g., Corbetta and Shulman, 2002). Another counterexample to the separation of these attention networks is present in two other areas found to be active in both the conflict and orienting contrasts. Left BA 6 and bilateral BA 37 were both implicated in conflict and orienting. However, the lack of a significant finding in the conjunction analysis suggests that activations within these general regions were not strictly colocalized across the subtractions. Furthermore, common activations were found for alerting and conflict in both the thalamus and left fusiform gyrus.

With these exceptions noted, the overall pattern suggests that even when measured in the same subjects during the same task blocks, alerting, orienting, and conflict functions of attention activate somewhat distinct cortical and subcortical anatomical networks. Overall, the finding that few, if any, neural substrates are shared by the three components of this task fits with our previous findings of no within-subject correlations on any of the three indexes. These results help to support our efforts to supply a single, simple test that can measure individual differences in the efficiency of several different brain networks involved in attention.

Acknowledgments

Supported by NSF grant BCS 9907831 and by a DeWitt Wallace-Reader's Digest Research Fellowship in Psychiatry. The authors would like to thank Drs. Yihong Yang, Hong Gu, Michael Worden, and Amir Raz for their help.

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