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Dissociated deficits in attentional networks in social anxiety and depression

Haoyu Wang¹, Ce Mo^{4,5*} & Fang Fang^{1,2,3*}

¹*School of Psychological and Cognitive Sciences and Beijing Key Laboratory of Behavior and Mental Health, Peking University, Beijing 100871, China;*

²*IDG/McGovern Institute for Brain Research, Peking University, Beijing 100871, China;*

³*Peking-Tsinghua Center for Life Sciences, Peking University, Beijing 100871, China;*

⁴*Center for Studies of Psychological Application, School of Psychology, South China Normal University, Guangzhou 510631, China;*

⁵*Institut des Sciences Cognitives Marc Jeannerod, Centre National de la Recherche Scientifique, UMR 5229, Bron 69675, France*

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A critical cognitive symptom that is commonly involved in social anxiety and depression is attentional deficit. However, the functional relationship between attentional deficit and these two disorders remains poorly understood. Here, we behaviorally disentangled the three key attentional components (alerting, orienting, and executive control) using the established attentional network task (ANT) to investigate how social anxiety and depression are related to deficits in these attention components. We identified a double dissociation between the symptoms of social anxiety and depression and the attentional component deficits when processing non-emotional stimuli. While individuals vulnerable to social anxiety exhibited deficits in the orienting component, individuals vulnerable to depression were impaired in the executive control component. Our findings showed that social anxiety and depression were associated with deficits in different attentional components, which are not specific to emotional information.

attentional networks, social anxiety, depression, orienting, executive control

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INTRODUCTION

Among anxiety and mood disorders, social anxiety disorder (SAD) and major depression disorder (MDD) are the two most prevalent disorders that affect a large population and elicit considerable societal costs (Cerdá et al., 2008; Wittchen et al., 1994). A common cognitive symptom of SAD and MDD is attentional deficit (Mathews and MacLeod, 2005; Peckham et al., 2010; Yiend, 2010), which is typically reflected as attentional bias, i.e., the inclination of

focusing on potential environmental threats or the difficulty of disengaging from negative information during attention processing (Koster et al., 2004). Despite the critical involvement of attentional deficits in SAD and MDD revealed in previous studies (Amir et al., 2009; Bar-Haim et al., 2007; Clark and Wells, 1995; Dalgleish et al., 2003; Eysenck et al., 2007; Heimberg et al., 2010; Hofmann, 2007; Mogg et al., 1992), how attentional deficits are related to these disorders remains less understood.

An important aspect of this question is the specificity of attentional deficits in SAD and MDD to emotional information (Mogg and Bradley, 2018; Soutschek and Schubert, 2013). However, so far there is no conclusive answer to

*Corresponding authors (Ce Mo, email: mocheck@sina.com; Fang Fang, email: ffang@pku.edu.cn)

whether attentional deficits in these disorders are specific to emotional information, as previous studies of attentional bias (Adólfsson et al., 2008; Johnson et al., 2008; Konrad et al., 2006), schizophrenia (Nestor et al., 2007; Wang et al., 2005) and Alzheimer's disease (Fernandez-Duque and Black, 2006). Importantly, unlike previous clinical studies that focused on diagnosed patients (Amir et al., 2009; Dalgleish et al., 2003; Mogg et al., 1992), we instead investigated the sub-clinical population that is more widely distributed along the spectra of SAD and MDD, thereby extending the understanding of attentional deficits in these disorders beyond the clinical population.

For example, in a classical dot probe paradigm, a neutral face and a negative face were simultaneously presented at equal horizontal distance from the central fixation point, after which subjects were required to detect a dot probe that were presented at the location of either face. It was found that subjects performed better at detecting the dot probe presented at the negative face location than that at the neutral face location. However, this effect might be caused by the sensitivity to the negative face, or by the difficulty of orienting attention resource to the probe regardless of its location. More recently, Hankin et al. (2010) reported that anxious and depressive participants exhibited attentional bias only to threat-related or negative stimuli, e.g., angry or sad faces. Furthermore, Kircanski et al. (2015) found that attention processing differed when processing faces of different emotions. However, findings from other studies suggested that attentional costs in anxious and depressive participants were not modulated by emotional valence (Kaiser et al., 2003; Rossignol et al., 2012; Yoon et al. 2015).

One possible reason for the inconsistency in these findings is that previous studies employed differed in experimental paradigms and attention effect measurements, which might thus tap into different subsets of attention components. According to the neurocognitive model of attention (Petersen and Posner, 2012; Posner and Petersen, 1990), the attention system itself is not unitary but is comprised of three functional networks: alerting, orienting and executive control. The alerting network is responsible for achieving and maintaining a state of alertness. The orienting network is mainly involved in the selection of input information, and the executive control network (or equivalently the conflict network) resolves response conflicts by maintaining attention to the target and inhibiting distractors. Further complicating the matters is that social anxiety and depression frequently co-occur (Kessler et al., 2005) and covary (Kendall and Watson, 1989) in terms of their affective states, rendering it difficult to understand the cognitive-behavioral correlates of these disorders.

In the current study, we used the attention network test (ANT) (Fan et al., 2002, 2009) to investigate deficits in different attention system components in subclinical individuals with high vulnerability to SAD and MDD. This paradigm provides an effective way of behaviorally dissociating and measuring the contribution of the three networks when processing non-emotional stimuli, thus providing direct insights into the specificity of attention network deficits to emotional information in these disorders. Notably, ANT has been widely employed in various clinical studies, including attention deficit hyperactivity disorder

RESULTS

We first examined whether the three attention networks could be identified at the behavioral level by calculating the alerting, the orienting (including engaging and disengaging) and the conflict effects using the formulae in the Method section. Consistent with previous findings, we found that all three effects were significant across participants (alerting effect: $t_{(75)}=5.87$, $P<0.001$; disengaging effect: $t_{(75)}=13.64$, $P<0.001$; engaging effect: $t_{(75)}=22.94$, $P<0.001$; conflicting effect: $t_{(75)}=24.47$, $P<0.001$), suggesting that the three attention networks could be effectively dissociated using the ANT paradigm. Notably, our findings were not confounded by difficulty difference across conditions, as there was no significant difference in accuracy among the no cue (mean \pm SEM: 96.74% \pm 4.31%), the double cue (95.40% \pm 4.72%) and the spatial cue (96.30% \pm 4.94%) conditions (one-way ANOVA: $F_{(2, 301)}=1.61$, $P=0.20$).

We then investigated which attention networks were involved in SAD and depression, respectively. We found that the four groups differed significantly in the orienting effect (One-way ANOVA: $F_{(3, 72)}=5.05$, $P=0.003$) and the conflict effect ($F_{(3, 72)}=3.24$, $P=0.027$), while there was no significant group difference in the alerting effect ($F_{(3, 72)}=1.30$, $P=0.28$), suggesting little involvement of the alerting network in either social anxiety or depression (Figure 1A). Interestingly, results of post-hoc comparisons revealed a clear double dissociation between the attention networks and the symptoms of these two disorders. Specifically, we found that both CMD group and HSA group exhibited stronger orienting effect in comparison to the CTL group (two-sample t test: HSA group: $t_{(37)}=-3.20$, $P=0.002$; CMD group: $t_{(44)}=-2.73$, $P=0.008$, multiple comparisons corrected), while no difference was found between the CTL group and the HD group. We also found that the HD group and the CMD group exhibited stronger conflict effect than the CTL group (two-sample t test: HD group: $t_{(49)}=-2.12$, $P=0.039$; CMD group: $t_{(44)}=-3.02$, $P=0.003$, multiple comparisons corrected), while the CTL group and the HSA group did not significantly differ in the conflict effect. Furthermore, given that the orienting effect was comprised of the disengaging effect

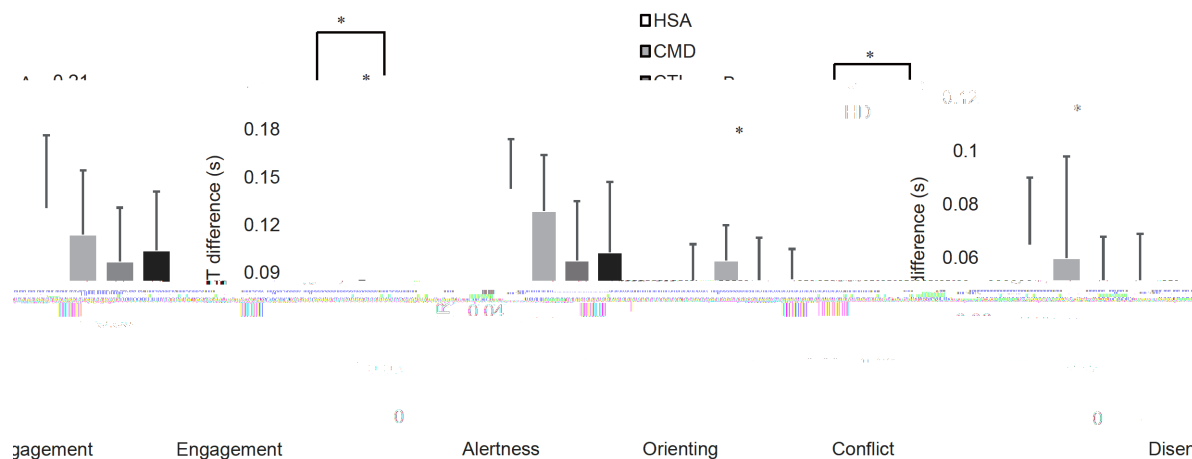


Figure 1 Effects of (A) the three attentional networks and (B) the orienting network component (engagement and disengagement) measured using reaction time (RT) difference in the four participant groups. Error bars denote one standard error of the mean across subjects. *, $P < 0.05$.

and the engaging effect, we performed similar analyses on these two effects respectively to further elucidate the involvement of the orienting network in social (Figure 1B). We found that the four participant groups differed significantly in the disengagement effect ($F_{(3, 72)} = 3.33$, $P = 0.024$) but not in the engagement effect ($F_{(3, 72)} = 3.33$, $P = 0.024$). Notably, both the HSA group and the CMD group exhibited stronger disengagement effects than the CTL group (HSA group: $t_{(37)} = -2.37$, $P = 0.020$; CMD group: $t_{(44)} = -2.31$, $P = 0.024$), while no significant difference was observed between the HD group and the CTL group ($t_{(49)} = 0.18$, $P = 0.861$). These findings combined to suggest that social anxiety and depression were associated with deficits in the orienting network and the executive control network, respectively. In particular, for the individuals with social anxiety, the orienting network deficit might mainly lie in the difficulty in disengaging from previous attention targets. To provide a more comprehensive characterization of the attention network effects, we also measured the effects of the three attentional networks based on the ratio index (Hu et al., 2013) and compared them across the participant groups. This analysis yielded highly consistent results with that based on RT differences. We found that the four groups differed significantly in the orienting effect (one-way ANOVA: $F_{(3, 72)} = 4.25$, $P = 0.008$) and the conflict effect ($F_{(3, 72)} = 2.98$, $P = 0.037$) with no significant group difference in the alerting effect ($F_{(3, 72)} = 1.49$, $P = 0.22$). Results of post-hoc comparisons also revealed a clear double dissociation between the attention network deficits and the symptoms of the two disorders (Figure 2). Specifically, both the HSA group and the CMD group exhibited stronger orienting effects than the CTL group (HSA group: $t_{(37)} = -3.55$, $P = 0.001$; CMD group: $t_{(44)} = -2.72$, $P = 0.009$), while no significant difference was found between the HD group and the CTL group ($t_{(49)} = -0.65$, $P = 0.518$). The HD group and the CMD group also yielded stronger conflict effects than the CTL group (two-

sample t test: HD group: $t_{(48,97)} = -2.14$, $P = 0.038$; CMD group: $t_{(44)} = -2.55$, $P = 0.014$, multiple comparisons corrected), while the CTL group and the HSA group did not significantly differ in the conflict effect. This suggested that our reported findings were not contingent on RTs, but were commonly reflected in different behavioral performance measurements.

Having identified the attention network deficits that are related to SAD and MDD, we further investigated the relationship between the severity of social anxiety and depression symptoms and the deficits of the two attention networks. To this end, a linear regression analysis was conducted with the SPS score as the dependent variable and the disengagement effect as the independent variable. Participants' age, gender, STAI-T and BDI scores were also included as covariates of no interest in the linear regression model. We found that the model explained a significant portion of the SPS score variance ($F_{(4, 79)} = 8.389$; $R^2_{\text{adjust}} = 0.308$; $P < 0.001$), and more importantly, SPS score positively correlated with the disengagement effect (partial correlation: $r = 0.343$, $P = 0.002$; Figure 3A). Further, we conducted another similar linear regression analysis, with the BDI score as the dependent variable and the conflict effect as the independent variable. We found that the BDI score variance could be well explained by the linear model ($F_{(5, 78)} = 9.771$; $R^2_{\text{adjust}} = 0.425$; $P < 0.001$), with a positive correlation between the BDI score and the conflict effect ($r = 0.362$, $P = 0.001$; Figure 3B). Together, these findings suggested that individual severity of depression and social anxiety could be predicted from the difficulty of reorienting and maintaining attention resources, respectively.

DISCUSSION

The present study aimed at investigating the relationship

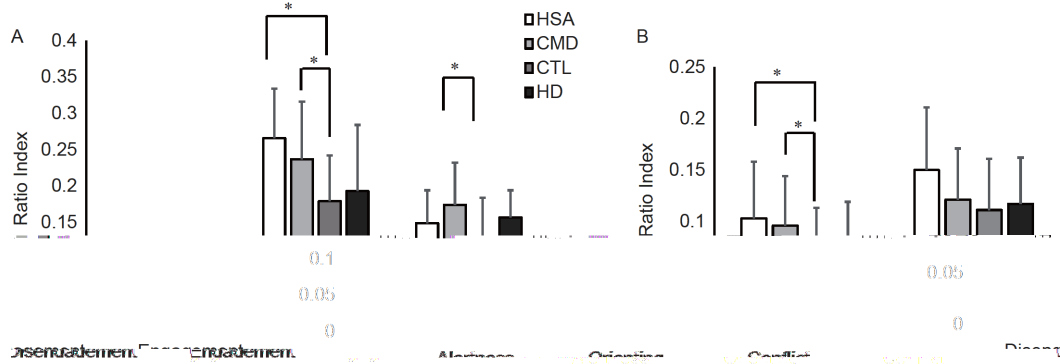


Figure 2 Effects of (A) the three attentional network and (B) the orienting network component (engagement and disengagement) measured using the ratio index in the four participant groups. Error bars denote one standard error of the mean across subjects. *, $P < 0.05$.

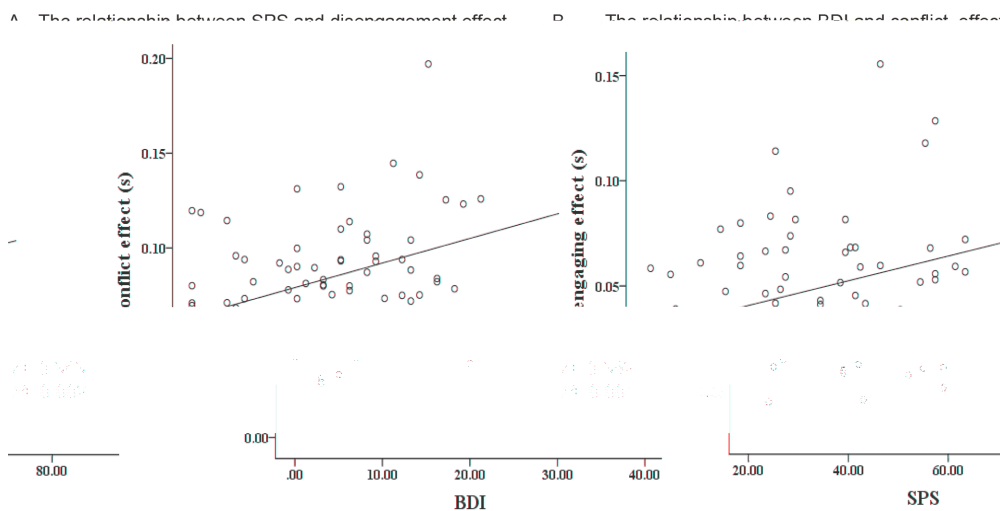


Figure 3 Relationships between clinical symptoms and the attentional components. A, Correlation between social anxiety symptom measurement (SPS scores) and the disengagement effect. The disengagement effect was calculated by subtracting the mean RT of the double-cue conditions from the valid-cue conditions ($RT_{\text{double cue}} - RT_{\text{valid cue}}$). B, Correlation between depression symptom measurement (BDI) and the conflict effect. The conflict effect was calculated by subtracting the mean RT of the incongruent conditions from the congruent conditions ($RT_{\text{incongruent}} - RT_{\text{congruent}}$).

between social anxiety and depression and attention system (McNally, 2016). At the neural level, previous fMRI findings have identified the involvement of right parietal cortex, a critical region in the orienting system (Calder et al., 2007; Xuan et al., 2016), in social anxiety (Gentili et al., 2016; Irle et al., 2014). Our study extended these findings by elucidating the exact component of the orienting system that was related to social anxiety symptoms, namely the disengagement component. We tentatively proposed two possible explanations for this finding. Impaired orienting ability might be a critical etiological factor of SAD, which rendered it difficult for social anxious individuals to disengage from relevant threatening social information in daily life, thus causing excessive anxiety. Notably, orienting ability could be regarded as a congenital trait (Posner et al., 2012; Rothbart et al., 1988; Manfredi, 2009). In autistic and anxiety disorder patients, it was also found that social anxiety symptoms were associated with the orienting network inefficiency (Bryson et al., 2004; Heeren et al., 2015; Heeren

et al., 2011). Infants with high orienting ability quickly learned to withdraw their attention away from sources of anxiety or distress, which was considered as an important emotional regulation strategy acquired in the early developmental stage

(Posner and Rothbart, 2007; Rothbart et al., 1992). These early temperamental characteristics might reflect the maturity of specific neural networks (Rothbart and Rueda, 2005). Alternatively, orienting network deficit might be the secondary symptom and maintenance factor, rather than the pathogenesis, of social anxiety. Social anxiety might be caused by negative social events (such as social rejection or bullying) in early life, which in turn leads to the attentional bias for social and emotional threats (Fung and Alden, 2016). Such bias might be further generalized to non-emotional stimuli as a result of attentional processing plasticity.

Our findings also suggested that subclinical individuals that are vulnerable to depression exhibited deficits in the executive control network, which was consistent with the typical symptoms of concentration difficulties (APA, 2013; Watts and Sharrock, 1985). Furthermore, Kaiser et al. (2003) suggested a specific deficit in response inhibition of depression patients. It was also found that rumination, a cognitive symptom of depression, was caused by impaired inhibitory control (Hester and Garavan, 2005; De Lissnyder et al., 2010). Neuroimaging studies suggested that depression was associated with hypoactivation in dorsolateral prefrontal cortex (DLPFC) and anterior cingulate cortex (ACC) (Davidson et al., 2002), which play a critical role in executive control (Smith and Jonides, 1999). Activation in regions involved in executive control was found attenuated in MDD patients during emotional task (Siegle et al., 2006; Wang et al., 2008). Together with these previous studies, our present findings indicated an impairment of inhibition in depressive individuals.

Notably, we did not find significant effect of age on any of the three attentional network effects, which was inconsistent with previous findings that age correlates with attentional components (Abundis-Gutiérrez et al., 2014; Williams et al., 2016). One possible reason is that the participants in our study were highly similar in age and educational background (i.e., college students), rendering it difficult to reveal the possible influences of age on the identified attention networks. In addition, the generalizability of our findings might also be constrained by the exclusion of other cognitive factors, such as intelligence, which might influence individual's attentional processing efficiency (Westlye et al., 2011) in our analyses. Further investigation is needed to investigate whether and how other cognitive factors might interact with attentional processing.

In summary, our findings showed that social anxiety symptoms were associated with the deficit in disengaging attention from irrelevant stimuli, while depression symptoms were related to deficits in executive control. Our findings suggested that social anxiety and depression might be mediated by deficits in different attentional components.

METHODS

Participants

Eighty college students with no diagnosed physical diseases (27 males; mean age \pm SD=22.41 \pm 2.95 years) were recruited online to participate in the study. Candidates were initially screened for psychotic disorder or other illnesses associated with cognitive dysfunction, current substance abuse or dependence, and serious suicidal tendency, via the mini-international neuropsychiatric interview (MINI; Sheehan et al., 1998), a structured interview assessing specific DSM-IV axis I disorders. All participants had normal or corrected-to-normal vision and had not received psychological or psychiatric treatment or psychotropic medications for at least one year. Written consents were collected in prior to the experiment. The experimental protocol was approved by the Ethical Committee of the Psychological Science Research Institute of Peking University.

Participants' symptoms of social anxiety and depression were assessed using Social Phobia Scale (SPS; Mattick and Clarke, 1998; Ye et al., 2007) and Beck Depression Inventory (BDI-II; Beck et al., 1996), respectively. In addition, we also measured participants' anxiety-proneness using State and Trait Anxiety Inventory-Trait version (STAI-T; Spielberger et al., 1983). Participants were then classified into four groups according to the scores of the two scales: (1) the high social anxiety (HSA) group (SPS \geq 60 and BDI<15); (2) the high depression (HD) group (SPS<60 and BDI \geq 15); (3) the comorbidity (CMD) group in which the individuals exhibited high social anxiety level and high depression level (SPS \geq 60 and BDI \geq 15); (4) the healthy control (CTL) group (SPS<60 and BDI<15). Detailed participant information in each group is shown in Table 1.

Stimuli and experimental procedure

The experiment was conducted in a dimly lit and quiet room.

Table 1 Demographic and clinical information of four participant groups

Variables	Groups				Group difference statistics
	HSA	HD	CMD	CTL	
<i>N</i>	9	21	16	30	
Age (mean \pm SEM)	23.22 (2.99)	22.67 (2.76)	22.06 (3.04)	22.21 (2.95)	$F_{(3, 72)}=0.41, P=0.74$
Male ratio	22.22%	28.57%	31.25%	41.18%	$\chi^2_{(3)}=2.89, P=0.41$

Visual stimuli were presented on an IYAMA HM204DT 21.5 inch CRT monitor (refresh rate=60 Hz, resolution: 1024×768, background luminance=21.30 cd m⁻²). Subjects viewed the stimuli from a distance of 65 cm with their heads stabilized on a chin rest. Each trial started with a cue display for 100 ms in which two cue boxes were presented on the left and the right side of the central fixation, respectively. The experiment consisted of three cueing conditions: the no cue condition in which neither cue box flashed, the double cue condition in which both cue boxes flashed, and the spatial cue condition in which only one cue box flashed. Following a variable cue duration (0, 400, or 800 ms, mean=400 ms), the target stimuli were presented at the location of either cue box for 500 ms. The target stimuli comprised of five left or right arrows arranged in a row with the central arrow as the probe and the other four as flankers, which subtended 3.6° in visual angle. Specifically, for the spatial cue condition, the flash cue signaled the location of the upcoming target in 75% of the trials (valid), whereas in the remaining 25% of the trials the target appeared at the opposite location of the cue (invalid) (Figure 4). For all cueing conditions, the probe was either in the same (50% chance, the congruent target) or the opposite direction (the incongruent target) as the flankers. Participants were instructed to identify the direction of the central probe. Trials were presented in a randomized order with the inter-trial interval ranged from 200 to 500 ms with a mean of 400 ms. Each participant completed four or eight blocks of 50 trials for each condition.

Data analysis

Data of four participants was excluded from group analysis due to high error rates (>20%) or failure to complete the experiment. For each participant, we excluded the trials in which the response was incorrect (~3.01%) or was made in less than 200 ms or more than 1,700 ms, and the trials whose RT exceeded two standard deviations from the mean in each condition. We then measured the effects of the three attention networks as previously described by Fan et al. (2009):

$$\begin{aligned} \text{Alerting} &= RT_{\text{no cue}} - RT_{\text{double cue}} \\ \text{Orienting} &= \text{Engaging} + \text{Disengaging} = (RT_{\text{double cue}} - RT_{\text{valid cue}}) + (RT_{\text{invalid cue}} - RT_{\text{double cue}}), \\ \text{Conflict} &= RT_{\text{incongruent}} - RT_{\text{congruent}} \end{aligned}$$

Specifically, the alerting effect characterizes the difficulty of activating the alertness state. The orienting effect consists of the engagement effect and the disengagement effect, which characterizes the difficulty of orienting attention resources to and away from a specific spatial location, respectively. The conflict effect characterizes the difficulty of inhibiting irrelevant information. In addition, we also measured the effects of the three attention networks using the ratio index (Hu et al., 2013):

$$\text{Alerting} = (RT_{\text{no cue}} - RT_{\text{double cue}}) / RT_{\text{double cue}}$$

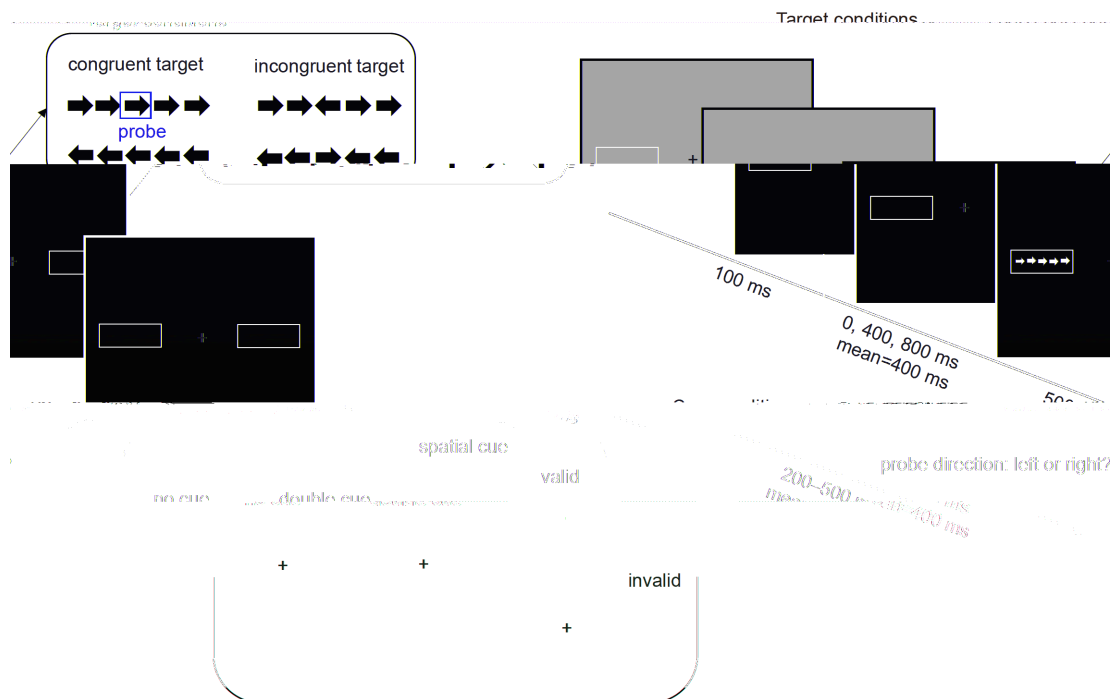


Figure 4 (Color online) Trial procedure of the ANT-R test (adapted from Fan et al., 2009). At the beginning of each trial, a cue display corresponding to one of the three possible cue conditions was presented for 100 ms, which involved one, two or no flashed cue boxes (shown in inset). After a variable duration of 0, 400, or 800 ms, one of four possible target stimuli (shown in inset) was presented inside one of the cue boxes for 500 ms. Specifically, for the spatial cue condition, the target stimuli could appear in the same or the opposite cue box with respect to the flash. Subjects' task was to discriminate the direction of the probe (red rectangle) at the center of the target stimulus.

$$\text{Orienting} = (\text{RT}_{\text{double cue}} - \text{RT}_{\text{spatial cue}}) / \text{RT}_{\text{spatial cue}}$$

$$\text{Conflict} = (\text{RT}_{\text{incongruent}} - \text{RT}_{\text{congruent}}) / \text{RT}_{\text{congruent}}$$

Compliance and ethics *The author(s) declare that they have no conflict of interest.*

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