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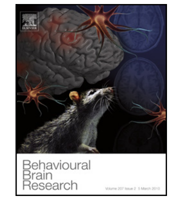

Research report

Parsing the intrinsic networks underlying attention: A resting state study

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HIGHLIGHTS

- We tested the efficiency of attentional networks.
- We estimated resting state networks.
- Attentional efficiency in distinct networks correlates with resting state networks.
- The brain owns intrinsic functional organization to support attentional components.

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ABSTRACT

The attention system functionally modulates brain activity to exert control over thoughts, feelings and actions. Three distinct but mutually interacting components of attention have been hypothesized: alerting, which mediates the maintenance of a state of vigilance toward an upcoming stimulus; orienting, which supports the selection of sensory information, and executive control that is involved in detecting and resolving cognitive conflicts. The performance of tasks probing these components engages fronto-parietal and thalamic regions. Also, general attention has been associated with the activity of resting-state networks (RSNs), which are sets of brain regions with synchronous temporal fluctuations. Importantly, the association between the intrinsic brain activity of RSNs and the efficiency and integration of the specific attentional components remains largely unexplored. For this aim, we recruited twenty healthy volunteers who performed the Attention Network Test-Revised (ANT-R), assessing the alerting, orienting and executive control components as well as their interactions, and underwent resting-state functional magnetic resonance imaging. For each participant RSNs were estimated using double regression. The RSNs spanning across areas previously implicated in attentional processing were correlated with ANT-R scores using multiple regressions. Significant brain behavior correlations emerged between ANT-R scores and RSNs comprising the regions relevant for attentional processing, i.e., left and right prefronto-parietal (PFC-PC), dorsal attentional (DAN), salience (SN), and default mode (DMN) networks. The activity of PFC-PC networks was correlated with alerting in parietal and frontal regions, and with location conflict in the frontal regions. The DAN connectivity was correlated with flanker, location conflict, and their interaction in parietal regions. SN was associated with flanker by location and flanker by orienting interactions in the inferior frontal regions. Finally, the activity of the DMN was associated with flanker conflict in midline structures such as precuneus and anterior cingulate cortex and also in right angular gyrus. These results suggest that the brain is endowed with an intrinsic functional organization to support attention, not only in its global function, but also in its distinct components.

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1. Introduction

Attention can be conceptualized as the system that modulates brain activity in order to exert control over thoughts, feelings and actions. According to Posner and Fan's model [1], the attention system includes three separate functions: alerting, orienting, and executive control, which work in a relatively independent way to modulate behavior in order to better adapt to environmental demands. These components are thought to be mediated by distinct neural systems [2–4] and neurotransmitter signaling pathways [5–7]. Specifically, alerting is pivotal for the achievement and the maintenance of a state of vigilance toward an impending stimulus; this function is subserved by fronto-parietal cortex and thalamus and influenced by the norepinephrine system. Orienting supports the selection of sensory information and the allocation of attention to relevant stimuli among several choices. This component is mediated by parietal cortex, frontal eye fields, superior colliculus and thalamus and modulated by the cholinergic system. Executive control, modulated by dopaminergic transmission, is supported by the anterior cingulate cortex, mainly responsible for cognitive conflict detection, and the lateral prefrontal and orbitofrontal cortices that are involved in conflict resolution and inhibitory control [1].

In support to this theory, a wealth of studies indicates that specific brain networks subserve attentional subcomponents during attentional and cognitive tasks [8]. Most strikingly, Fan and colleagues demonstrated that even when measured during the same task (i.e., the Attention Network Test, ANT), the alerting, orienting and conflict functions activate separable and distinct fronto-parietal and thalamic regions [3], supporting the idea that the three components of attention are subtended by separable anatomical networks.

However, while early studies posited that the different features of cognition are attributable to the isolated operations of single brain areas, increasing evidence suggests that the brain is organized in distinct large-scale systems and that cognition would emerge from the dynamic interactions of different networks, spanning across several functionally connected brain regions [9]. A recent approach proposed for the identification of these networks is resting state functional magnetic resonance imaging (RS-fMRI). In this approach, intrinsic networks are identified using the temporal coherence of the low-frequency fluctuations (0.01–0.1 Hz) observed in the blood-oxygen level dependent (BOLD) signal, in distinct brain areas. Several studies have demonstrated the functional relevance of most RSNs, through the association between network connectivity and behavioral performance [10,11]. Importantly, these networks can be consistently identified not only during the execution of a task, but also at rest: the patterns of activity related to task performance are similar to those identified during resting state [12–15], and changes in the cerebral blood flow associated with task performance can account for less than 5% relative to rest [16]. Thus, the resting state brain already possesses most of the information extractable from the hemodynamic response, which may reveal properties of the cerebral intrinsic wiring [17,18] without the confounding effects due to differences in performance.

The neural networks underlying the three components of attention are relatively unexplored. To our knowledge, only one study investigated the activity of one neural network associated with alerting and executive control, as measured by the ANT [19]. However, this study focused only on a fronto-parietal network function, thus leaving unclear the role of other attentional RSNs potentially relevant for cognitive functioning, including attentional processing. Indeed, prefronto-parietal (PFC-PC) network has been associated with cognitive conflict detection and resolution [20]; dorsal attentional network (DAN) has been described as a cortical system with functionally specialized portions supporting specific processes for attentional control and it has been related to the exertion of top-down influences on visual areas during the orientation of attention toward significant events [21,22], which are mainly detected among negligible stimuli via the salience network SN; [23]. Lastly, the default mode network (DMN) has been implicated in the allocation of cognitive resources for the execution of a task [24] and its altered function has been associated with neurodevelopmental disorders with significant attentional deficits such as attention-deficit/hyperactivity disorder (ADHD) [25–28].

In addition, recent evidence suggests that the three attentional components, although endowed with distinct functions and supported by distinct neural substrates, could interact with each other [29,30]. For instance, alerting improves overall response speed but can interfere with executive control, and cognitive conflict resolution is differentially affected by diverse orienting cues. Such subtle yet significant interactions can be detected at the behavioral level using a revised version of the ANT (ANT-R), but the neural correlates of such interactions have not been investigated hitherto.

The present study aimed at identifying the individual role of the various intrinsic brain networks in mediating each attentional component and their interactions. First, we assessed the efficiency of attentional processing at the behavioral level in a group of healthy subjects using the ANT-R, a task specifically designed to parse out the alerting, orienting and executive control components of attention as well as their interactions. Second, we analyzed fMRI data collected during resting state in the same group of healthy subjects to evaluate the RSNs that are thought to be associated with attention. Third, we examined the relationship between behavioral indexes of attentional performance and intrinsic brain activity.

2. Materials and methods

Twenty adult subjects (age, 39.7 ± 8.6 years; 7 females; education, 13.9 ± 3.8 years) were recruited from the local community to participate in this study. All subjects were free from any psychiatric, neurological or medical condition, as established through a standard clinical interview, and gave written informed consent to the study. Participants underwent two separate experimental sessions: a behavioral attention task and a functional magnetic resonance imaging (fMRI) scanning. The local ethics committee of Parma (Italy) approved the study protocol.

2.1. Behavioral attention task

Subjects performed the Attention Network Test Revised (ANT-R; [29]), a behavioral task designed to measure the efficiency of the three attentional networks (see Fig. S1). The ANT-R results from the combination of the classic Posner task [31] and a flanker task [77] and represents an improved version of the classic ANT [32], developed to detect elusive but significant interactions and integrations among the attentional networks. These improvements are achieved with several modifications of the classical ANT, including manipulations of cue conditions (no cue, double cue, spatial cue), cue validity (valid, invalid), target conditions (congruent, incongruent), cue–target intervals (0, 400, 800 ms), and an additional cognitive conflict measure (location congruency of target).

Subjects are asked to indicate as quickly and accurately as possible the direction of the target that is the central arrow. During the flanker condition, two pairs of arrows are presented with the target: they can point in the same direction (flanker congruent condition) or in the opposite direction relative to the target (flanker incongruent condition). Also, if the location of the target arrow is consistent with its pointing direction (location congruent), faster responses are expected, if not the condition is defined location incongruent (location conflict).