Attention to Neglect

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Patients with spatial neglect fail to attend to stimuli in the contralesional visual world. He et al. used fMRI to reveal how disrupted functional connectivity, independent of task-evoked activation, in ventral and dorsal attentional networks may explain behavioral impairment in neglect and recovery from acute neglect.

Spatial neglect is a clinically spectacular and theoretically provocative syndrome. Patients with spatial neglect fail to perceive and to respond to stimuli in the field opposite to their lesion (contralesional). In the acute stages, especially after right-sided lesions, the neglect can be florid, with patients failing to dress the left halves of their bodies, to shave or make-up the left halves of their faces, to eat from the left halves of plates while complaining about small servings, and failing to copy the left halves of clocks, flowers, and other objects placed centrally before them. When writing to dictation, such patients use only the right half of a pad of lined paper, or when walking to another room they travel in long series of right-hand turns when a simple left-hand turn would bring them directly to their destination. This remarkable neglect of the opposite half of the world can occur without any deficit in visual perception. In this issue of *Neuron*, He et al. (2007) report a major advance in our understanding of the brain basis of attention through an innovative use of functional magnetic resonance imaging (fMRI) with patients with spatial neglect.

The phenomenon of spatial neglect has attracted inventive experiments aimed at understanding the neuropsychological nature of the neglect. Studies have shown that patients neglect not only the left half of the world before their eyes, but also the left half of their imagination of familiar places (Bisiach and Luzzatti, 1978). A stimulus that rotates from the neglected field into the intact field remains neglected, as if the neglect, once applied mentally, travels with the stimulus into the intact half of the world (Behrmann and Tipper, 1994). After the acute or florid phase of spatial neglect, a chronic phase may remain in which a patient perceives a stimulus presented in the contralateral field but fails to perceive the leftward stimulus when stimuli are presented simultaneously in both fields (attention to stimulus in the good field extinguishes attention to the bad field). When such a patient was shown faces simultaneously in both visual fields during functional neuroimaging, he was conscious of the left-field faces for only a third of the presentations. He exhibited activation of right primary visual cortex (V1) regardless of whether he consciously perceived the face but exhibited activation of parietal and frontal areas only for left-field faces that were consciously perceived (Vuilleumier et al., 2001). These studies indicate that neglect does not occur early in perception but rather later in high-level representations of space mediated by frontoparietal cortices.

A theoretically influential analysis of neglect employed a paradigm used to study normal attention (Posner et al., 1984). In this task, people simply press a button when a simple target stimulus appears on the left or right half of a display. In the neutral condition, a fixation appears centrally prior to the target stimulus. On other trials, an arrow appears centrally pointing toward the left or right. On "valid" trials (typically 75% of the arrow trials), the arrow points to the side where the stimulus will appear shortly—this warning enhances the speed of response to the stimulus. On "invalid" trials (typically 25% of the arrow trials), the central arrow points in the incorrect direction—this misleading warning slows response speed by directing attention in the wrong direction. Surprisingly, patients with chronic contralateral neglect following cortical injury take normal advantage of the valid arrows, even when the arrow points them toward their neglected field. These trials show that the patients can engage and move their attention even into the neglected field with a salient cue. These patients, however, are greatly impaired when an invalid central arrow has pointed their attention to their intact field and the stimulus then appears in the neglected field. The patients could not disengage their attention from the intact field. Their attention, once drawn to their ipsilesional field, became stuck in quicksand.

He et al. (2007) examine brain function in patients with spatial neglect in a novel and fruitful way. Their investigation builds on the discovery that fMRI can reveal brain functions not only during task-evoked performance, but also during rest—when people simply lay in a scanner and let their minds wander freely. During rest, there are fluctuations in blood-oxygenation level-dependent (BOLD) signals that are correlated in anatomically specific and widely distributed systems. Functional connectivity is defined by the strength of correlated fluctuations between brain regions. For example, there is strong functional connectivity within two anatomically distinct frontoparietal attentional systems (Fox et al., 2006). A dorsal attentional network that includes bilaterally the intraparietal sulcus and frontal eye fields may guide spatial attention in the contralateral visual field. A right-lateralized ventral attentional network that includes the temporoparietal junction and ventral frontal cortex may mediate target detection and reorientation. Thus, these spontaneous and correlated fluctuations may identify naturally interacting networks of the brain.

In prior research using task-evoked BOLD responses, this group suggested that spatial neglect may be a consequence of structural injury to the ventral network, which results in a functional imbalance between structurally intact dorsal networks, with a hyperactive left dorsal network dominating a hypoactive right dorsal network (Corbetta et al., 2005). This model integrates what had been an apparent paradox between the behavioral expression of neglect, which seems to reflect dysfunction of the dorsal attentional pathway and mounting evidence that the lesions most associated with neglect are actually in the temporal (ventral pathway) lobe (Karnath et al., 2001).

The present study examined fluctuations of BOLD signals with task-evoked responses statistically removed in eleven patients during both their acute and chronic stages of recovery. In addition, attentional and disengagement deficits were measured behaviorally in the patients to provide a quantitative measure of neglect. Functional connectivity in early (retinotopic) visual cortex was intact in the patients, consistent with the view that neglect exerts its effect in later-stage, higher cortical zones. Functional connectivity in the ventral network was disrupted at both acute and chronic stages, consistent with the idea that brain regions that are structurally damaged are less likely to functionally recover (although there was a suggestion of partial recovery in this network from task-evoked activations). The degree of ventral system connectivity correlated with broad attentional deficits (errors and slowness in both visual fields), consistent with the idea that the right ventral system mediates an aspect of spatial attention that applies to both visual fields (just as a left ventral system mediates language abilities in both visual fields). In the anatomically intact dorsal attention system, connectivity between left and right parietal cortices was disrupted in the acute stage but fully recovered in the chronic stage, and the degree of disruption correlated with the magnitude of the contralateral disengagement deficit. These disruptions were further related to injuries of white matter tracts, measured by diffusion tensor imaging (DTI), that structurally connect frontotemporal and frontoparietal cortices. The disruptions of functional connectivity in both systems were correlated with each other and with the behavioral deficits, which supports the view that the interaction of the ventral and dorsal systems underlies the neglect.

This is an impressive and important study. It is impressive because it involves longitudinal study of well-characterized patients, a daunting task. The investigators had to assess a number of measurement issues, such as whether the presence of a lesion affected the BOLD response, which serves as the hemodynamic index of neural processes in fMRI. If a lesion altered vasculature function, then the BOLD response would be a misleading index of neural activation. The investigators examined these and other potential confounds associated with scanning patients with noteworthy care.

The study is important for several reasons. First, it enhances our understanding of both the normal organization of spatial attention and its impairment in neglect through an increasingly precise and complete model of anatomy, functional networks, and behavior. Second, it encourages the view that BOLD functional connectivity at rest reveals the integrity of neural networks that mediate behaviors. The close and specific relations between the two different attentional networks and different behavioral outcomes strengthen the putative relation between resting brain measures and active behaviors. Third, the study elegantly associates anatomical damage in one region with dysfunction in related but anatomically intact other regions.

Many neurological diseases, and perhaps many psychiatric diseases, may also be characterized by a combination of structural injury and resultant dysfunction in structurally unaffected brain regions that, in combination, produce a behavioral syndrome. The appeal of the resting scan is that it simply requires a patient to lie still in the scanner—the patient does not have to understand instructions or perform a difficult task. Thus, resting scans are increasingly used to study a wide range of diseases. An open question has been how resting scans may relate to normal or abnormal behaviors—does the brain doing nothing at rest reveal a functional neural architecture relevant for the brain in action? One important caveat in the present study is that task-evoked activations were statistically controlled, so further studies will need to make certain that functional connectivity measured during true rest (without any task involved) yields similarly strong relations to behavioral dysfunction. The present study provides exciting evidence that the resting scan can indeed shed novel and informative light on the specific neural mechanisms that mediate behavior and clinical disorders of behavior.

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