Look Before You Reach!

This issue of *Neuron* contains an elegant neuroimaging study by Prado and colleagues, who report that the network of brain areas involved in visually guided reaching is modulated by whether targets are presented in central or peripheral vision. These results clarify prior inconsistencies in the literature regarding reach-related activation in the human brain, and they are valuable in interpreting neuropsychological cases of patients who demonstrate misreaching.

In most everyday situations, you likely look toward locations to which you reach, though certainly it is possible to make reaching movements, albeit less accurately, to targets that you're not looking at. For example, you may flick off a light switch on the way out the door without needing to explicitly look at it. Research in neuropsychological patients suggests that different brain regions are involved in reaching actions depending on where the gaze is directed. In the disorder of optic ataxia, patients with damage to parietal cortex have problems with reaching, such that their hand misses the target (Perenin and Vighetto, 1988). However, misreaching typically only occurs when the patient sees the target in peripheral vision; when the patient can look directly at the target, reaching is accurate.

In this issue of *Neuron*, Prado and colleagues (Prado et al., 2005) show that the network of brain areas activated by visually guided reaching changes in neurologically intact human subjects depending on whether the eyes look directly at the target before the reach. With the use of functional magnetic resonance imaging (fMRI), they compared three conditions in which subjects reached out to touch a dot that was illuminated on a screen. The conditions differed in the instructions to the subject about where to look. Each condition was compared to a control condition with the same gaze instructions but no reaching movement. In one condition, subjects were instructed to look at the target before reaching to it. Activation was observed in several regions, including the medial intraparietal sulcus (mIPS) and dorsal premotor cortex (PMd). In another condition, subjects were instructed to keep their gaze fixed on a point and not look at the target before reaching. Now activation was observed in an additional area, the parieto-occipital junction (POJ), as well as the other reach-related areas. Moreover, the extent of PMd activation was greater than in the first condition. In the final condition, the target disappeared after a fraction of a second, and before reaching, subjects were instructed to look at the location where the target had been. In this case, the target had been presented in peripheral vision, but after the saccade, the eyes were directed to the location where the reach would unfold. This case also produced activation in POJ as well as mIPS, and it produced greater activation in PMd than the first condition. Taken together, these results suggest that mIPS was activated by reaching, regardless of the subjects' gaze; whereas, when the target location had been initially encoded in peripheral vision, POJ became active and PMd became more active. The authors suggest that POJ and PMd activation depend critically on whether the target had been successfully "captured by the fovea" prior to offset.

These results agree well with a recent paper (Karnath, 2001) that used new lesion analysis techniques to revisit the common lesion site in optic ataxia (Perenin and Vighetto, 1988). They reported that optic ataxia typically resulted from lesions in the vicinity of either POJ or mIPS. Prado et al.'s new fMRI results predict that ataxic patients with POJ lesions that spare mIPS should benefit from looking at reach targets, whereas ataxic patients whose lesions include mIPS should demonstrate misreaching regardless of gaze.

An extensive literature has suggested that the eye and hand are closely coupled. Eye movements typically precede hand movements and improve their accuracy. The authors suggest that POJ may be involved in decoupling eye-hand coordination. Their results also provide an intriguing interpretation of bizarre neuropsychological cases such as "magnetic misreaching" in which parietal patients instructed to reach to a peripheral target instead reach to the location where they're looking (Carey et al., 1997; Jackson et al., 2005). By this account, parietal patients who demonstrate magnetic misreaching would presumably have lesions in POJ, leading to an inability to decouple reach from gaze.

This experiment helps to clarify a somewhat confusing literature of prior neuroimaging studies on reaching (for a review, see Culham et al., 2005). Experiments using positron emission tomography (PET) have typically studied reaching with free viewing and reported activation typically only in the vicinity of mIPS. In contrast, experiments that use fMRI have typically studied pointing, in which the subject directs the index finger in the direction of the target without actually extending the arm, rather than reaching because pointing induces fewer hand-motion artifacts in fMRI. These experiments have typically found activation around both mIPS and POJ. It was possible that the pointing activation in POJ was due to the nature of the task. That is, pointing is mostly used for communication rather than action (for example, one would point to show that "there is a mosquito there on your arm" but would reach to brush it off) and thus may invoke different systems. However, Prado et al.'s fMRI study of true reaching with direct viewing of the targets demonstrates that the critical variable is the retinal location of target presentation rather than the nature of the hand action. Furthermore, their Supplemental Data (see their Figure S1) illustrates the stereotaxic coordinates of prior reaching and pointing studies and nicely shows that POJ was only activated when targets were presented peripherally, whereas mIPS was activated regardless of gaze.

These results may also elucidate the determination of homologies between macaque monkey and human parietal regions, if indeed such homologies exist. Although prior fMRI studies have suggested possible human equivalents of the parietal reach region (Connolly et al., 2003) and its subdivisions (Grefkes et al., 2004), Prado and colleagues' results suggest that there may be not one but multiple reach-related regions in the human brain. The challenge now is to determine what distinguishes the various areas and whether the areas show clear functional equivalencies with the known macaque areas (including the medial intraparietal sulcus and V6A

areas, which together form the parietal reach region). Such comparisons would be informed by macaque neurophysiological studies of reaching to stimuli presented in peripheral versus foveal vision.

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Selected Reading

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