Journal Club

Editor's Note: These short reviews of a recent paper in the *Journal*, written exclusively by graduate students or postdoctoral fellows, are intended to mimic the journal clubs that exist in your own departments or institutions. For more information on the format and purpose of the Journal Club, please see http://www.jneurosci.org/misc/ifa_features.shtml.

Weight Lifting in the Human Brain

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Review of Jenmalm et al. (http://www.jneurosci.org/cgi/content/abstract/26/35/9015)

The world, just like us, is constantly changing. Making predictions about what will happen to you when you do something (and correcting these predictions based on what is actually happening) is therefore of vital importance. An influential theory states that the brain solves this challenge by using forward models: while you grasp an object, the anticipated sensory consequence of your action is compared with the actual sensory input. If there is an error, e.g., because you think the object is heavy and it turns out to be light, a corrective signal is sent back to the motor cortex to quickly adapt the motor command.

Although there is ample psychophysical evidence for forward models (for review, see Wolpert and Ghahramani, 2000), and the concept may extend to explaining even some forms of psychiatric behavior (Frith et al., 2000), the neural architecture responsible for these computations is still not fully understood. Jenmalm et al. (2006) have made a significant contribution to this topic using functional magnetic resonance imaging in a study recently published in the *Journal of Neuroscience*.

The authors instructed participants to lift an object with their right hand, using the tips of their index fingers and thumbs. On some trials, the weight of the object changed unpredictably: a light object became heavier or a heavy object became lighter. These weight changes were effectuated by the experimenter adding or removing an extra weight, outside the scanner, that was connected to the object that had to be grasped. During the experiment, force and position signals, as well as acquisition times of each scan were recorded simultaneously. This sophisticated experimental setup allowed the authors to compare behavioral performance and brain activity with event-related functional magnetic resonance imaging during lifting trials in which the weight unpredictably changed to trials when there was no weight change. Consistency and robustness of differences in brain activity was ensured by taking into account intersubject variability in the statistical model and correcting the results for multiple comparisons in an a priori search space based on independent data.

From a theoretical point of view, when the weight changes unpredictably, the predicted sensory feedback and the actual sensory feedback do not match. Therefore, the module comparing the predicted and actual sensory feedback will generate an error signal. By contrasting brain activity during trials with a weight change to trials in which no such change took place, the authors could localize this "comparator node."

Weight changes led to increased activity in the right inferior parietal cortex [Jenmalm et al. (2006), their Fig. 3 (http://www.jneurosci.org/cgi/content/full/26/35/9015/F3)]. A previous study shows that disruption of the posterior parietal cortex by means of transcranial magnetic stimulation interferes with the ability to quickly correct a movement on the basis of new sensory information (Desmurget et al., 1999). Together, these data and the location and connectivity of this region, receiving input from sensory cortices and having output connections to the motor regions, make it a good candidate for "comparator region."

There were also differences in brain activity that were specific to the direction of the weight change. The left primary sensorimotor cortex became more active when the weight was increased and less active when the weight was decreased [Jenmalm et al. (2006), their Fig. 4*A* (http://www.jneurosci.org/cgi/content/full/26/35/9015/F4)]. The right cerebellum had an opposite, inhibitory role: it became more active when the weight was decreased and less active when the weight was increased [Jenmalm et al. (2006), their Fig. 4*B* (http://www.jneurosci.org/cgi/content/full/26/35/9015/F4)]. These activities likely reflect the actual force corrections of the right hand that had to be performed and their sensory consequences. This is consistent with the excitatory and inhibitory roles of the primary sensorimotor cortex and cerebellum, respectively, in the control of movements.

Although the study of Jenmalm et al. advances our understanding of where the different nodes that interact during movement corrections are located, the "how question" is still open: that is, how do these brain regions interact to generate these fast corrective responses? To understand this, we have to look at the dynamics of the system and investigate how the inferior parietal cortex, the cerebellum, and the primary sensorimotor cortex interact.

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One possible mechanism is that the predicted sensory consequence and actual sensory feedback are compared in the inferior parietal lobe and, from this region, a corrective signal is sent to the primary sensorimotor cortex and cerebellum. At present, this is pure speculation. However, new analysis methods, such as dynamic causal modeling (Friston et al., 2003) aiming at describing the interaction between brain regions, could help to elucidate these interactions.

The study by Jenmalm et al. is an excellent building block for future studies, because it allows focusing on the target regions identified in this study. Understanding their interactions will now be a major goal for future neuroimaging studies.

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