

Structure and Function Come Unglued in the Visual Cortex

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In this issue of *Neuron*, Chowdhury and DeAngelis report that training monkeys to perform a fine depth discrimination abolishes the contribution of signals from area MT to the execution of a different, coarse depth discrimination. This result calls into question the principle of associating particular visual areas with particular visual functions, by showing that such associations are modifiable by experience.

The architecture of extrastriate visual cortex in primates has been studied for decades. We now know at least two dozen richly interconnected visual cortical areas outside primary visual cortex in both monkeys and humans (Van Essen et al., 2001). A great quest of systems neuroscience has been to identify the functions performed by each area. Figure 1 shows a schematic representation of these areas in the macaque monkey and their connections. Broad divisions of function suggested by lesion studies led to an initial division into parallel dorsal and ventral “streams” of areas (Ungerleider and Mishkin, 1982; color coded in Figure 1), and the years since have seen many studies seeking to connect areas and functions more precisely by linking behavioral measures of vision to data obtained with three biological approaches: (1) neurophysiological assessment of neuronal selectivity, sensitivity, and association with behavioral choice; (2) lesion or pharmacological methods to inactivate regions of cortex; and (3) electrical microstimulation techniques to activate regions of cortex artificially. The poster child for the success of these methods is visual motion perception, which has been robustly associated with activity in dorsal stream area MT by all three methods: (1) the high prevalence of directionally selective neurons in MT immediately suggests a role for this area in visual motion processing, the motion sensitivity of MT neurons closely matches behavioral sensitivity in monkeys, and MT neuronal activity is related to behavioral choice in a motion discrimination; (2) MT lesions selectively impair motion discrimination; and (3) MT microstimulation affects behavioral judgments

of motion (Newsome et al., 1990, 1995).

The signal success of this work led many to think that similar strategies could be used to link other visual functions to other areas, so that each box in a diagram like Figure 1 could in time be labeled, like an old map (“here be motion,” “here be color,” “here be dragons”), to identify its particular role in vision. But the case of motion and MT may be misleading. Visual motion signals are strongly prevalent only in MT and a few nearby, closely related areas, limiting the potential source of signals for motion perception. Selective responses to most other features of visual stimuli, however, are widespread in the extrastriate visual cortex (Merigan and Maunsell, 1993). So it should not come as a surprise that it has proved difficult to reproduce this initial success in another domain.

Consider stereoscopic vision, which extracts the 3D structure of visual scenes from the differences between the projections of the visual world onto the two retinas. Neurons in all areas of visual cortex are usually activated by stimuli delivered to either eye, and many are also sensitive to binocular disparity, the proximal geometric cue to stereoscopic depth (Cumming and DeAngelis, 2001). So it is not obvious that one would expect to associate any particular area with stereoscopic depth perception. Performance on a “coarse” stereoscopic judgment task can be influenced by microstimulation of MT (DeAngelis et al., 1998), showing that signals in MT can influence judgments of depth. Perhaps more surprisingly, inactivating MT with a local injection of muscimol disrupts coarse stereopsis, suggest-

ing that this area plays a critical rather than merely a contributory role (Uka and DeAngelis, 2006). But it emerges that all forms of stereopsis are not created equal—in the same study, Uka and DeAngelis showed that inactivating MT does not affect performance on “fine” stereoscopic judgments.

What are “coarse” and “fine” stereopsis, and why do they give such different results? The stimuli for both coarse and fine stereopsis consist of the same elements, isolated dots at particular locations in depth defined by their disparity with respect to a fixation point. But how these dots are assembled in the two cases is different (see Figure 1 of Chowdhury and DeAngelis, 2008). For coarse stereopsis, most dots form a 3D cloud extended in depth both in front and behind the fixation plane, all drifting across the field. Within this cloud, other dots define a flat surface that is either nearer or farther than the fixation plane, and the monkey must decide whether the surface is near or far. The disparity of the surface is quite large, hence the term “coarse”; performance is controlled by adjusting the fraction of dots in the noise cloud. For fine stereopsis, the dots define two surfaces: a central circle of drifting dots and a surrounding annulus of static ones. Both surfaces are out of the fixation plane, and the monkey’s task is to indicate whether the inner circle is in front or behind the surround. Performance is controlled by varying the disparity difference between the surfaces; the smallest discriminable disparities define the limit of fine depth discrimination, hence the term “fine.” So both the stimuli and the tasks are quite different: (1) coarse stereopsis requires only

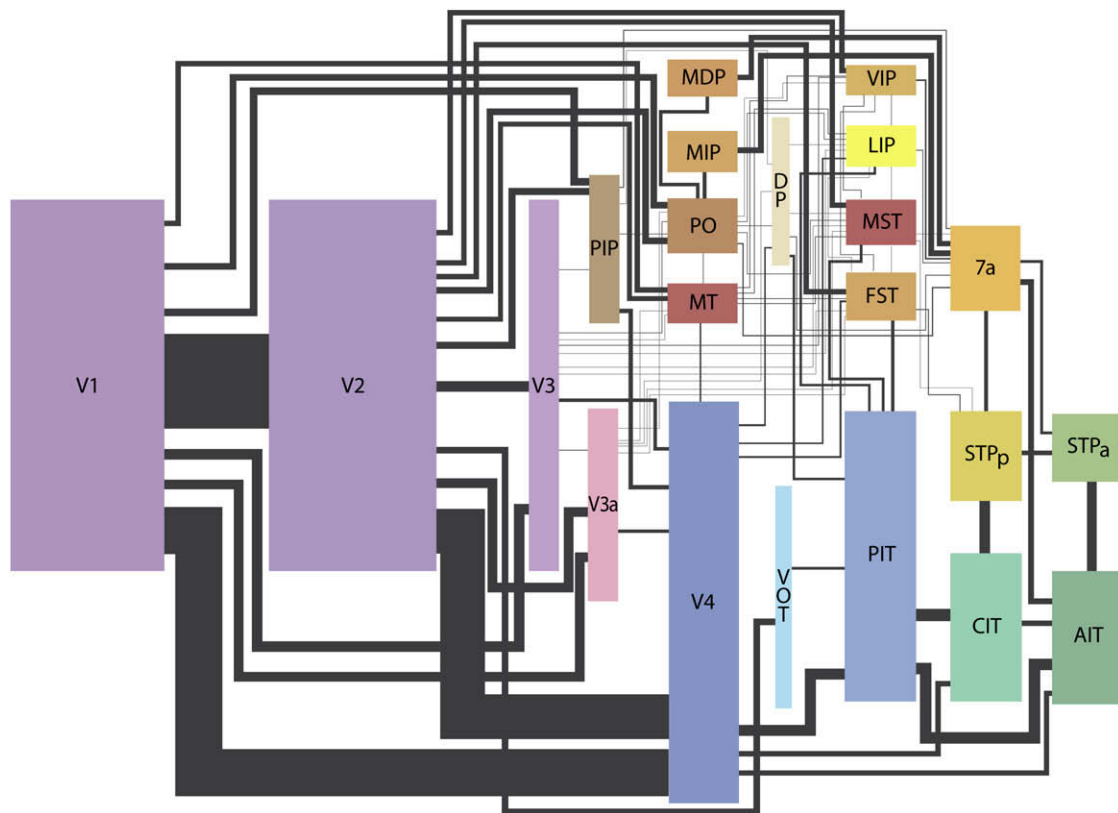


Figure 1. A Scaled Representation of the Cortical Visual Areas of the Macaque

Each colored rectangle represents a visual area, for the most part following the names and definitions used by Felleman and Van Essen (1991). The gray bands connecting the areas represent the connections between them. Areas above the equator of the figure (reds, browns) belong to the dorsal stream. Areas below the equator (blues, greens) belong to the ventral stream. Following Lennie (1998), each area is drawn with a size proportional to its cortical surface area, and the lines connecting the areas each have a thickness proportional to the estimated number of fibers in the connection. The estimate is derived by assuming that each area has a number of output fibers proportional to its surface area and that these fibers are divided among the target areas in proportion to their surface areas. The connection strengths represented are therefore not derived from quantitative anatomy and furthermore represent only feedforward pathways, though most or all of the pathways shown are bidirectional. The original version of this figure was prepared in 1998 by John Maunsell.

an *absolute* depth judgment with respect to fixation, while fine stereopsis requires the judgment of *relative* depth, i.e., comparing depth across space; (2) the particular coarse stereopsis task used requires the monkey to discriminate a signal in noise, while the fine task does not; (3) the range of disparities is quite different.

Chowdhury and DeAngelis (2008) replicate the finding that monkeys initially trained on coarse stereopsis show impaired coarse depth discrimination when muscimol is injected into MT. Remarkably, the same animals, after a second round of training on fine stereopsis, are unimpaired at *either* fine or coarse depth discrimination by similar injections. Moreover, recordings in MT show that neuronal responses are not altered by learning the fine stereopsis task. Given the differences between the tasks and the large number

of visual areas containing disparity-sensitive neurons, one might not be surprised to find different areas involved in the two tasks. But it is quite unexpected that merely learning one task would change the contribution of areas previously involved in the other. Chowdhury and DeAngelis conclude that the change in outcome reflects a change in neural decoding—decision centers that decode signals to render judgments of depth, finding MT signals unreliable for the fine stereopsis task, switch their inputs to select some better source of disparity information. Candidates include ventral stream areas V4 or IT, where relative disparity signals have been reported (Orban, 2008) and which contain far more neurons than MT (Figure 1). When challenged afresh with the coarse depth task, these same decision centers may now find that

their new sources of information can solve the coarse task as well as the old ones. MT is no longer critical.

Perhaps in other monkeys MT would never have a role in stereopsis at all. Chowdhury and DeAngelis' monkeys were trained simultaneously or previously to discriminate motion, which engages MT. Faced with a qualitatively similar random dot stimulus, it might make sense for the cortex to try to solve the new problem of stereopsis with existing decoding strategies. But if the animals were initially trained on a different task—say, a texture discrimination—MT might never be engaged at all. It would also be interesting to see the outcome if monkeys were trained on depth tasks that were less different and could be interleaved in the same sessions, for example noise-limited depth judgments using similar absolute or relative disparity

cues. Muscimol injection could then be used to ask whether animals could switch between sensory representations from moment to moment, as well as from month to month.

Perhaps the most surprising thing about the results of Chowdhury and DeAngelis is that they surprise us. Visual cortex is chock-full of cells sensitive to binocular depth (Cumming and DeAngelis, 2001; Orban, 2008). Why should we expect cells in just one area to be critical for depth perception? We can perhaps trace the blame back to Lettvin et al. (1959), the famous paper whose title “What the frog’s eye tells the frog’s brain” implicitly asserts that signals from a neuron selective for some feature exist de facto to support behavioral responses to that feature. But this is teleology. We don’t learn the purpose of a neuron—or

an area full of neurons—by measuring its selectivity. For that, we must make direct measurements of the relationship between neuronal activity and behavior. Put simply, even though neuronal signals in some area may tell all we want to know about some feature, that fact alone is no reason to assume that the cells downstream are actually listening.

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The Hippocampus and Dopaminergic Midbrain: Old Couple, New Insights

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Humans have a natural ability to gain new insights by generalizing from previous experience. In this issue of *Neuron*, Shohamy and Wagner reveal how generalizations naturally emerge during associative learning through a partnership between putatively dopaminergic circuitry in the midbrain and the hippocampus.

Deriving new knowledge from past experiences can arguably be viewed as one of the most far reaching capabilities of human memory. Niels Bohr, the venerated Danish physicist, is an impressive example: his first quantum model of the atom published in 1913, is an innovative synthesis of the ideas of Planck, Einstein, and Rutherford. How, then, does the human brain accomplish such feats? In their paper in this issue of *Neuron*, Shohamy and Wagner (2008) approach an important aspect of this puzzling question, our ability to efficiently generalize past ex-

perience to new situations, based on hidden threads that cut across multiple events.

One possibility is that generalization is accomplished when it is needed: that means, when faced with a problem that requires generalization, this calls into play the effortful recall and subsequent on-line manipulation and comparison of individual exemplars or past experiences. While empirical evidence suggests that such “retrieval-based” generalizations may be important in some situations (Heckers et al., 2004), there is a more adaptive

and proficient way of achieving the same goal: this is to detect and to encode generalizations as events around us unfold over time and store these generalizations as memories. The beauty of such a mechanism is that it makes generalizations available when they are needed without requiring the effortful “retrieval-based” route. The possibility of such a mechanism is exciting, but so far its identity and operating mechanisms have remained elusive. Now, Shohamy and Wagner (2008) have discovered such a mechanism and termed it “integrative encoding.”