But while the decline in information content per response is therefore inevitable, the sharp decline in informational redundancy is not, and it is very interesting to consider what the reasons and the purpose behind this redundancy reduction might be. Ed Rolls' VisNet model of cortical visual object processing also exhibits a redundancy reduction at successively higher levels of the processing stream. There the redundancy reduction arises as higher levels of the network become sensitive to increasingly abstract feature combinations. In the VisNet model, redundancy reduction is therefore a hallmark of a transition from a "feature-based" to an "object-based" representation, and it is intriguing to speculate that the redundancy reduction in the auditory pathway described by Chechik et al. (2006) might similarly be interpreted as the fingerprint of a transition from an acoustic-based feature toward a more "auditory object-based" representation.

The VisNet model is not "born" with a low-redundancy representation of its stimuli in its top layers. The redundancy reduction only arises after a competitive learning process in which higher layers become sensitive to specific feature combinations (Rolls and Treves, 1998; Rolls, 1995). One might predict that the low-redundancy representations observed at the levels of the auditory cortex may similarly be the result of developmental or learning mechanisms which decorrelate the responses of individual cortical neurons. This could easily be tested by measuring redundancy in the cortex of young, naive animals with little auditory experience. Achieving a low-redundancy representation in auditory cortex could well be an important part of learning how to hear.

Jan Schnupp[1]
[1] Department of Physiology, Anatomy, and Genetics
Sherrington Building
University of Oxford
Oxford OX1 3PT
United Kingdom

Selected Reading

Chechik, G., Anderson, M.J., Bar-Yosef, O., Young, E.D., Tishby, N., and Nelken, I. (2006). Neuron *51*, this issue, 359–368.

Elliffe, M.C., Rolls, E.T., and Stringer, S.M. (2002). Biol. Cybern. *86*, 59–71.

Escabi, M.A., Miller, L.M., Read, H.L., and Schreiner, C.E. (2003). J. Neurosci. *23*, 11489–11504.

Garcia-Lazaro, J.A., Ahmed, B., and Schnupp, J.W. (2006). Curr. Biol. *16*, 264–271.

Klein, D.J., Depireux, D.A., Simon, J.Z., and Shamma, S.A. (2000). J. Comput. Neurosci. *9*, 85–111.

Nelken, I., Rotman, Y., and Bar Yosef, O. (1999). Nature *397*, 154–157.

Nelken, I., Chechik, G., Mrsic-Flogel, T.D., King, A.J., and Schnupp, J.W. (2005). J. Comput. Neurosci. *19*, 199–221.

Rolls, E.T. (1995). Behav. Brain Res. *66*, 177–185.

Rolls, E., and Treves, A. (1998). Neural Networks and Brain Function (Oxford, England: Oxford University Press).

Schnupp, J.W., Hall, T.M., Kokelaar, R.F., and Ahmed, B. (2006). J. Neurosci. *26*, 4785–4795.

Wang, X., and Kadia, S.C. (2001). J. Neurophysiol. *86*, 2616–2620.

DOI 10.1016/j.neuron.2006.07.016

The Lure of the Unknown

Using event-related fMRI, Bunzeck and Düzel show that midbrain regions putatively housing dopamine cell bodies activate more for novel pictures than for negative pictures, pictures requiring a motor response, or repeated pictures. These findings indicate that midbrain regions preferentially respond to novelty and suggest that novelty can serve as its own reward.

Meriwether Lewis and William Clark spent years working at it, Edmund Hillary and Tenzing Norgay climbed Mt. Everest for it, Neil Armstrong flew into space for it, and Robert Falcon Scott died for it—a chance to discover something never before seen. A long tradition of human exploration testifies to the motivating force of novelty. Evolutionary biologists have argued that in order to flourish, all foraging species must have a drive to explore the unknown (Panksepp, 1998). How such a drive manifests in the brain, though, has remained unclear. In this issue of *Neuron*, for the first time, Bunzeck and Düzel (2006) show that midbrain regions that putatively house dopamine neurons preferentially respond to novel rather than rare, arousing, or behaviorally relevant stimuli (Bunzeck and Düzel, 2006).

From the outside, the ventral tegmental area (VTA) and substantia nigra (SN) are easy to miss. Nestled deep in a bend of the brainstem, these nuclei house the bodies of most of the dopamine neurons that innervate the striatum and prefrontal cortex. Tract tracing studies indicate that while the VTA projects to more ventral regions of the striatum and prefrontal cortex, the SN projects to more dorsal and lateral regions of the striatum and prefrontal cortex. Though small, these nuclei are in a position to exert widespread influence. Indeed, from the inside, life without these midbrain neurons is far from easy. For instance, both organic lesions (due to Parkinson's disease) and synthetic lesions (due to improperly manufactured drugs) of the SN/VTA lead to mental and physical immobility.

While lesion studies suggest that dorsal pathways innervated by the SN play a role in movement, ventral pathways innervated by the VTA play a less-understood role in motivation (Haber and Fudge, 1997). Some prominent theories hypothesize that activity in this ventral pathway confers "salience" upon stimuli (Berridge and Robinson, 1993). However, theorists have defined salience differently, confounding empirical attempts to isolate the function of these nuclei. For instance, some definitions of salience invoke novelty, others invoke behavioral relevance, and still others invoke arousal.

Here, Bunzeck and Düzel operationally define "salience" in four different ways. During acquisition of event-related fMRI, the investigators showed subjects pictures of faces or outdoor scenes embodying different attributes of salience and then measured the SN/VTA response to these different stimuli. A first group of pictures was novel, or never seen before. A second group of pictures was behaviorally relevant, requiring a button press. A third group of pictures was negative and thus presumed to be arousing (i.e., a negative expression in the case of faces, or a car accident in the case of scenes).

A fourth group of pictures were distinct but appeared more than once (called "neutral oddballs"). When not viewing one of these pictures, subjects saw a repeated neutral picture for the remaining two-thirds of the trials. Pictures appeared about every 3 s.

The investigators found that among all pictures, novel pictures most powerfully activated the SN/VTA, as well as parts of the hippocampus and striatum, suggesting that SN/VTA activation responded to novelty rather than other types of salience. Other types of pictures recruited other regions. Somewhat surprisingly, given the putative role of dopamine projections in movement, pictures requiring a motor response did not powerfully activate the SN/VTA regions, instead recruiting a motor circuit involving the red nucleus, thalamus, and motor cortex. Negative pictures also did not potently activate the SN/VTA, instead more robustly activating other midbrain regions (i.e., the locus coeruleus) and the amygdala. Finally, compared to the repeated picture, the neutral oddball activated the hippocampus, as well as other regions like the anterior cingulate.

The investigators also examined whether novelty enhances memory. Hippocampal activation has been associated with encoding memories in fMRI studies (Brewer et al., 1998; Wagner et al., 1998), and novel pictures activated this region as well as the SN/VTA. This leads to the inference that subjects should show superior memory for novel pictures. In fact, they did not. Instead, as in other research (Ranganath and Rainer, 2003), subjects remembered familiar pictures better than novel pictures. However, in a separate experiment, the investigators found an interesting contextual effect in which familiar pictures interspersed with novel pictures got a transient memory boost, detectable 20 min but not 1 day later. This finding can be contrasted with those of other recent studies which show that reward cues coactivate the SN/VTA and hippocampus, which enhances long-term memory not only for the cues (Wittmann et al., 2005), but also for pictures that follow them (Adcock et al., 2006).

Together, these findings potentially inform an exciting new body of research that attempts to link motivation and memory. A recent theory postulates that two circuits form a loop, by which novelty can promote memory (Lisman and Grace, 2005). In the first descending circuit, novelty activates the hippocampus, which synapses on the SN/VTA via subcortical pathways that pass through the ventral striatum. A second ascending circuit completes the loop, in which the activated SN/VTA releases dopamine in the hippocampus, promoting memorization of the novel stimulus. The present findings provide partial support for the loop theory. They are consistent with recruitment of the first circuit, in which hippocampus, striatum, and SN/VTA are activated by novelty. However, they are not consistent with recruitment of the second circuit, since novel stimuli were not better remembered. However, there was a transient boost in memory for familiar stimuli in the context of novel stimuli. Since other fMRI studies suggest that reward cues activate this second circuit, which corresponds with enhanced encoding of subsequent stimuli, it may be that novel stimuli themselves are not better remembered but put the brain in a receptive state for remembering what is yet to come (which could be a persisting novel stimulus or something else) (Dayan, 2002; Knutson and Adcock, 2005). Such a mechanism might prove highly useful to a predicting, foraging animal (Kakade and Dayan, 2002).

The findings also raise questions about the reward value of novel pictures. For instance, did subjects prefer novel pictures to less novel, negative emotional, or behaviorally demanding pictures? The study did not incorporate positive emotional pictures, which might provide an interesting future comparison with novel pictures. One could predict that both novel and positive pictures might separately activate the SN/VTA. Alternatively, if the novelty effects are mediated by the reward value of novelty, one might predict that positive pictures, embedded in the same experiment, might "steal" SN/VTA activation from novel stimuli.

In the face of continuing technological advance, challenges in visualizing SN/VTA activity with fMRI still remain. The SN/VTA are small, and although fMRI researchers have convincingly reported activation in these regions (Adcock et al., 2006; Knutson et al., 2005; Wittmann et al., 2005), smaller voxel sizes and spatial smoothing kernels are definitely in order. Additionally, the SN/VTA lie adjacent to a tissue interface and directly above the pulsating arteries of the circle of Willis, which visibly move especially these ventral regions of the brain (Dagli et al., 1999). Special means of dealing with the pulsations are under development and may reduce noise in these regions, including cardiac gated sampling during image acquisition (Guimaraes et al., 1998) or postacquisition filtering with the cardiac rhythm (Glover et al., 2000). Finally, as noted by many others (Logothetis and Wandell, 2004), increases in fMRI blood oxygen-level dependent (BOLD) signal pose an interpretive dilemma in whether they reflect incoming signals, outgoing signals, or some combination of the two. Recent electrophysiological studies are beginning to suggest that increased BOLD activation primarily indexes postsynaptic changes due to neural input, which naturally raises the question of which other regions inform the VTA about the arrival of a novel stimulus.

Exploration is not limited to physical frontiers and foreign lands. Galileo Galilei and Isaac Newton could likely identify with the excitement of peering for the first time into previously unknown worlds. By beginning to trace links between novelty, reward, and memory, Bunzeck and Düzel have given us a good start toward understanding the motivation that drives explorers and scientists alike.

Brian Knutson[1] and Jeffrey C. Cooper[1]
[1] Department of Psychology
Stanford University

Selected Reading

Adcock, R.A., Thangavel, A., Whitfield-Gabrieli, S., Knutson, B., and Gabrieli, J.D.E. (2006). Neuron *50*, 507–517.

Berridge, K.C., and Robinson, T.E. (1993). Brain Res. Brain Res. Rev. *18*, 247–291.

Brewer, J.B., Zhao, Z., Desmond, J.E., Glover, G.H., and Gabrieli, J.D.E. (1998). Science *281*, 1185–1187.

Bunzeck, N., and Düzel, E. (2006). Neuron *51*, this issue, 369–379.

Dagli, M.S., Ingeholm, J.E., and Haxby, J.V. (1999). Neuroimage *9*, 407–415.

Dayan, P. (2002). Trends Cogn. Sci. *6*, 105–106.

Glover, G.H., Li, T.Q., and Ress, D. (2000). Magn. Reson. Med. *44*, 162–167.

Guimaraes, A.R., Melcher, J.R., Talavage, T.M., Baker, J.R., Ledder, P., Rosen, B.R., Kiang, N.Y., Fullerton, B.C., and Weisskoff, R.M. (1998). Hum. Brain Mapp. *6*, 33–41.

Haber, S.N., and Fudge, J.L. (1997). Crit. Rev. Neurobiol. *11*, 323–342.

Kakade, S., and Dayan, P. (2002). Neural Netw. *15*, 549–559.

Knutson, B., and Adcock, R.A. (2005). Neuron *45*, 331–332.

Knutson, B., Taylor, J., Kaufman, M., Peterson, R., and Glover, G. (2005). J. Neurosci. *25*, 4806–4812.

Lisman, J.E., and Grace, A.A. (2005). Neuron *46*, 703–713.

Logothetis, N.K., and Wandell, B.A. (2004). Annu. Rev. Physiol. *66*, 735–769.

Panksepp, J. (1998). Affective Neuroscience: The Foundations of Human and Animal Emotions (New York: Oxford University Press).

Ranganath, C., and Rainer, G. (2003). Nat. Rev. Neurosci. *4*, 193–202.

Wagner, A.D., Schacter, D.L., Rotte, M., Koutstaal, W., Maril, A., Dale, A.M., Rosen, B.R., and Buckner, R.L. (1998). Science *281*, 1188–1191.

Wittmann, B.C., Schott, B.H., Guderian, S., Frey, J.U., Heinze, H.J., and Düzel, E. (2005). Neuron *45*, 459–467.

DOI 10.1016/j.neuron.2006.07.017