model assumes that attention enhances neural responses that are evoked by stimuli in a restricted region of visual space. Thus, the spotlight model predicts that the responses evoked by the edge configuration in the receptive field of **Figure 1c** should be equally enhanced when attention is directed to the white or to the dark square, as the receptive field is equally close to the focus of attention in both instances. However, in the new study[1], attentional modulation did not depend on spatial relationships, but instead depended on the neurons' border-ownership preference relative to the attended object. This agrees with human neuroimaging studies that show that attention can select not only regions of space, but also entire objects[6]. Therefore, border ownership is a likely neural substrate of object-based attention.

The idea that top-down processes act on local circuits or networks instead of individual cells might also help to resolve an ongoing debate about the role of attentional modulation in primary visual cortex. Single, isolated stimuli placed in the receptive fields of V1 neurons show little or no response modulation with attention[7]. However, greater attentional modulation is seen with more complex stimuli that provide context information[8,9]. The interface hypothesis may explain these discrepant findings. Complex stimulus arrays, but not single stimuli, engage local networks that represent context information, thereby providing the interface that is used by attentional mechanisms, resulting in robust attention effects. Thus, attentional modulation at a given processing stage in visual cortex may be best predicted by how much the attended stimulus engages local circuits. Also consistent with this idea, local interneurons (which subserve intrinsic circuits) receive stronger attentional modulation than other cell classes[10].

The interface hypothesis also converges well with the biased competition theory of attention[11]. When multiple stimuli are present at the same time in the visual field, they compete for neural representation in visual cortex. The neural substrate of this competition is a mutual suppression of neural responses[12], and this is another example of an automatic process that occurs without attention. When a stimulus is selected for further processing among multiple items, top-down processes appear to counteract the suppressive influences that are induced by nearby stimuli, and act to strengthen the neural representation of the attended stimulus[12,13]. These processes are typically observed at intermediate processing stages of visual cortex, such as in area V4 or MT. According to the interface hypothesis, these findings can be interpreted as competing stimuli engaging a local intrinsic circuit, thus providing an interface for the selection mechanisms to operate on. Thus, the interface hypothesis may provide a new framework for the interpretation of many empirical findings in the attention field.

In some respects, the interface hypothesis of attention is similar to another recent proposal[14]. Both hypotheses challenge the commonly held notion that attention acts in a hierarchical manner, which is based on the finding that attention effects are greater in extrastriate cortex than in early visual cortex. Instead, both proposals suggest that it is not a visual area's location in the processing hierarchy that determines the magnitude of attentional enhancement, but instead it is how involved the local circuits are in processing contextual scene information. The related proposal emphasizes the role of behavioral context, suggesting that a single visual area may perform many different functions depending on task demands. For instance, V1 neurons respond differently to the same visual stimuli depending on the type of behavioral task[14]. Attention is thought to gate the interaction of feedback connections from higher areas and local intrinsic networks, thereby strengthening connections that are important for the current behavioral context.

The idea that top-down selection mechanisms operate preferentially on intrinsic circuits and local networks not only provides an intriguing framework for explaining the role of top-down processes, but also raises a number of important issues that need to be addressed in future research. How do different interfaces, such as the segmentation circuit of early visual cortex and the competition circuit of later extrastriate cortex, interact[15]? Are the cellular mechanisms underlying attentional modulation of interface circuits the same across different visual-processing stages? Qiu *et al.*[1] have provided an important first step in revising some of our traditional notions of top-down selection mechanisms.

1. Qiu, F.T., Sugihara, T. & von der Heydt, R. *Nat. Neurosci.* **10**, 1492–1499 (2007).
2. Wertheimer, M. *Psychol. Forsch.* **4**, 301–350 (1923) [in German; English translation in Ellis, W. *A Source Book of Gestalt Psychology* (Routledge and Kegan Paul, London, 1938)].
3. Zhou, H., Friedman, H.S. & von der Heydt, R. *J. Neurosci.* **20**, 6594–6611 (2000).
4. Zipser, K., Lamme, V.A. & Schiller, P.H. *J. Neurosci.* **16**, 7376–7389 (1996).
5. James, W. *The Principles of Psychology* (Dover, London, 1890; reprinted 1950).
6. O'Craven, K. M., Downing, P. E., Kanwisher, N. *Nature* **401**, 584–587 (1999).
7. McAdams, C.J. & Maunsell, J.H. *J. Neurosci.* **19**, 431–441 (1999).
8. Ito, M. & Gilbert, C.D. *Neuron* **22**, 593–604 (1999).
9. Motter, B.C. *J. Neurophysiol.* **70**, 909–919 (1993).
10. Mitchell, J.F., Sundberg, K.A. & Reynolds, J.H. *Neuron* **55**, 131–141 (2007).
11. Desimone, R. & Duncan, J. *Annu. Rev. Neurosci.* **18**, 193–222 (1995).
12. Reynolds, J.H., Chelazzi, L. & Desimone, R. *J. Neurosci.* **19**, 1736–1753 (1999).
13. Kastner, S., De Weerd, P., Desimone, R. & Ungerleider, L.G. *Science* **282**, 108–111 (1998).
14. Gilbert, C.D. & Sigman, M. *Neuron* **54**, 677–696 (2007).
15. Beck, D.M. & Kastner, S. *Nat. Neurosci.* **8**, 1110–1116 (2005).

The optimistic brain

Daniel L Schacter & Donna Rose Addis

Faced with the metaphorical glass, most people see it as being half full. A new study shows that activity in two limbic areas, the rostral anterior cingulate cortex and amygdala, reflects an optimistic attitude.

Take a moment to consider the following questions. In uncertain times, do you usually expect the best? Do you expect more good things to happen to you than bad? Do you think that if something can go wrong for you, it will? Do you hardly ever expect things to go your way? People who respond "yes" to the first two questions and "no" to the latter two are characterized as optimists[1]. Most of us tend to be optimistic, which is a good thing because optimism is associated with many benefits to both physical and mental health; optimists tend to be well-adjusted psychologically and are equipped to handle stress well[2]. But we may be optimistic to a fault, in the sense that we maintain unrealistically positive expectations of our futures. For example, compared to the population in general, people think that they are more likely to own their own homes and live a long life and also think that

The authors are in the Department of Psychology, Harvard University, 33 Kirkland St., Cambridge, Massachusetts 02138, USA.
e-mail: dls@wjh.harvard.edu

they are less likely to have a drinking problem or a heart attack[3]. Although researchers have explored cognitive and social factors that contribute to optimistic bias and related mistakes that people make when predicting the future[4], next to nothing is known about the underlying brain processes. Sharot *et al.*[5] now report a neuroimaging study that sheds light on how the brain generates an optimistic bias.

Sharot *et al.*[5] analyzed functional magnetic resonance imaging scans from 15 young adults. During scanning, subjects were given brief descriptions of significant events, such as 'the end of a romantic relationship' or 'winning an award', and were cued to think about either a past event that had actually occurred or a future event that might occur. Because subjects cannot speak aloud in the scanner, they pushed a button when the memory of a past event or simulation of a future event began to take shape in their minds, and then again when the memory or simulation was fully formed. Subjects also rated how emotionally arousing the event was and judged the valence of the event (positive, neutral or negative). Then, after the scanning session, subjects provided additional ratings concerning their memories and simulations: how vivid they were, how strongly they felt that they were reliving their pasts or 'pre-experiencing' their futures, the time of the event, and their subjective sense of how close in time they felt to the event. Subjects also completed an optimism scale, using items similar to the questions that we asked at the beginning of this article[1].

Subjects said that positive future events felt closer in time than did negative future events, they rated positive events in the future as more positive than positive events from the past, and they also indicated that positive future events were more intensely 'pre-experienced' than negative future events. These effects were strongest in the most optimistic subjects. The functional magnetic resonance imaging results revealed a possible brain basis for these optimistic biases. Several regions showed similarly increased activity when subjects recalled past events and imagined future events, including areas in the frontal lobe and the posterior cingulate cortex. There was also substantial activation in the amygdala, a structure that has been linked with emotional memory. The amygdala, as well as a region toward the rostral (front) portion of the anterior cingulate (rACC) with which it is connected (**Fig. 1**), showed less activity when people imagined negative future events than with any of the other conditions (positive future events, positive past events or negative past events). When people imagined positive future events, the activities of the rACC and the amygdala were more strongly correlated with one another than when the subjects imagined negative future events. Notably, more optimistic individuals showed relatively greater rACC activation when imagining positive versus negative future events than did less optimistic individuals.

These findings provide clues concerning the neural underpinnings of optimistic bias by showing that areas involved in emotional processing selectively reduce their activity when people think about negative future events and coordinate activity when people think about positive future events; the effects are most pronounced in the most optimistic individuals. Furthermore, these results nicely bring together insights from several different areas of research.

Recent studies show that a similar network of brain regions is activated when people remember past experiences and imagine future events and that patients with memory deficits have difficulty imagining novel and future events (for a review, see ref. 6), suggesting that one function of memory is to generate simulations of possible future events that are used for making plans and predictions[4,6]. Although the results of Sharot *et al.*[5] generally fit with earlier neuroimaging studies, the authors did not report activation in the hippocampus, a structure that is critical for memory and is one of the regions that has shown robust activity when people remember past events and imagine future events[6]. This difference could be attributable to experimental design. Sharot *et al.*[5] compared remembering and imagining to an unconstrained baseline condition in which subjects fixated on a cross, rather than to a baseline condition involving an active control task; studies that use such an unconstrained baseline often fail to find evidence of hippocampal activation[7].

The results complement many previous findings that the amygdala is involved in emotional memory. For example, the amygdala activates selectively during both encoding and retrieval of emotional items compared with nonemotional items[8]. The extent of amygdala activity can even predict when people show memory distortions for emotional (versus nonemotional) experiences[9]. The findings of Sharot *et al.*[5] indicate that amygdala activation is also associated with the imagining of future emotional events. It is uncertain whether this activation is specific to emotional events, as subjects rated too few events as neutral to analyze. However, previous studies of imagining future events did not report amygdala activation, nor did they use highly emotional events[6]. It also remains to be determined whether amygdala activation is specific to imagining future emotional events or whether it is observed more generally during imagining of present or past events.

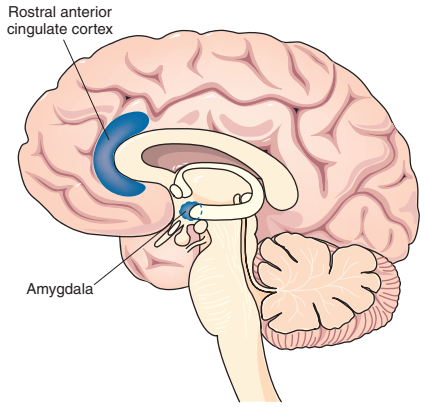


Figure 1 Sharot *et al.*[5] found two regions involved in optimism: the rACC, a strip of cortex surrounding the corpus callosum, and the amygdala, an almond-shaped structure located in the inner part of the temporal lobe. Both of these regions are closely interconnected and, along with other cingulate, medial temporal and subcortical regions, form the brain's emotional network, the limbic system. Sharot *et al.*[5] found that activity in both the rACC and amygdala was reduced when people thought about negative future events relative to positive future events or any past event. Moreover, the activity in these two regions was most strongly correlated when people imagined positive future events. Activity in the rACC correlated with trait optimism.

These results could provide clues about the nature of psychopathological conditions. Given that optimism is associated with psychological well-being[2] and that imagining positive outcomes for future events increases one's belief in the probability of a good outcome and decreases worry[10], it is not surprising that psychopathological disorders are associated with changes in future thinking. Depressed patients have difficulty providing specific details when they remember the past or imagine the future[11] and believe that positive future events are not likely to happen to them[12]. Pessimism is also involved in depression, with an increased anticipation of negative events[12].

Findings from functional and structural neuroimaging of mood disorders converge with the results reported by Sharot *et al.*[5]. Depressed patients show reduced volume and metabolism in the same subregion of the rACC[13] that Sharot *et al.*[5] found correlated strongly with optimism. When corrected for volume loss, metabolism in the remaining rACC tissue is actually elevated in patients relative to controls[13]. This finding appears to be dependent on mood state; rACC hyper-metabolism is evident in nondepressed adults during experimentally induced sadness, and, in patients, effective antidepressant treatment

reduces rACC metabolism to normative levels[13]. Thus, mood may be an important factor modulating the ability to engage the neural mechanisms that are associated with optimism bias, such as reduced rACC activity when thinking about negative future events.

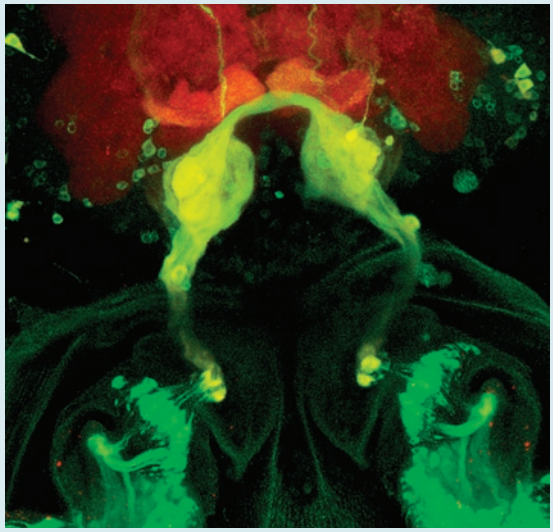
Although optimism is usually beneficial, it may not always promote adaptive behavior and can even be detrimental. Optimists may believe they will attain a goal even when they do not possess the ability to effectively pursue that goal[14] or to respond to setbacks that occur[15]. For instance, optimism is sometimes negatively correlated with academic achievement[14]. Moreover, it can lead to false beliefs that things will turn out well, which may explain why optimism can be associated with risky behavior[14]. Optimism can also lead to disappointment if one's high expectations are not realized. Indeed, there are times when it is maximally adaptive to shift from optimistic to more realistic, or even pessimistic, expectations, such as when goals are important or a negative outcome is probable[14]. In such instances, pessimism can facilitate preparedness and the use of strategies to reduce the occurrence or consequences of negative outcomes.

These limitations on the benefits of optimism make sense from the brain-based perspective suggested by Sharot *et al.*[5]. If optimism bias reflects a relative reduction of activity in emotional brain regions when we contemplate a negative future outcome, it is not surprising that sometimes our benign outlooks will prove misleading. In light of evidence that people shift to a more pessimistic outlook when a negative outcome is probable, this reduction might not occur when people imagine negative events that are likely to happen in the near future; in Sharot *et al.*[5], subjects imagined negative events that were not likely to happen anytime soon.

We agree with a previous study[15] that concluded on the basis of psychological evidence that, "People should be optimistic enough to take advantage of the many benefits of a positive outlook, but they should also sufficiently temper that optimism so that they can motivate preventative action and avoid being caught off guard." If the brain is often biased towards promoting a rosy vision of the future, a healthy dose of realism is required to keep the picture in balance.

1. Scheier, M.F., Carver, C.S. & Bridges, M.W. *J. Pers. Soc. Psychol.* **67**, 1063–1078 (1994).
2. Nes, L.S. & Segerstrom, S.C. *Pers. Soc. Psychol. Rev.* **10**, 235–251 (2006).
3. Weinstein, N.D. *J. Pers. Soc. Psychol.* **39**, 806–820 (1980).
4. Gilbert, D.T. & Wilson T.D. *Science* **317**, 1351–1354 (2007).
5. Sharot, T., Riccardi, A.M., Raio, C.M. & Phelps, E.A. *Nature* published online 24 October 2007.
6. Schacter, D.L., Addis, D.R. & Buckner, R.L. *Nat. Rev. Neurosci.* **8**, 657–661 (2007).
7. Stark, C.E.L. & Squire, L.R. *Proc. Natl. Acad. Sci. USA* **98**, 12760–12765 (2001).
8. Phelps, E.A. *Annu. Rev. Psychol.* **57**, 27–53 (2006).
9. Kensinger, E.A. & Schacter, D.L. *Neuropsychologia* **43**, 1429–1443 (2005).
10. Brown, G.P., Macleod, A.K., Tata, P. & Goddard, L. *Anxiety Stress Coping* **15**, 1–17 (2002).
11. Williams, J.M.G. *et al. Mem. Cognit.* **24**, 116–125 (1996).
12. Miranda, R. & Mennin, D.S. *Cognit. Ther. Res.* **31**, 71–82 (2007).
13. Drevets, W.C. *Biol. Psychiatry* **48**, 813–829 (2000).
14. Shorey, H.S. *et al. Psychol. Inq.* **13**, 322–331 (2002).
15. Sweeny, K., Carroll, P.J. & Shepperd, J.A. *Curr. Dir. Psychol. Sci.* **15**, 302–306 (2006).

Olfactory axons *derailed* in the brain



Yao *et al.* examine how sensory axons influence patterning of olfactory glomeruli in *Drosophila melanogaster* on page 1423 of this issue. Olfactory sensory neurons send their axons into the antennal lobes of the brain, where they synapse onto dendrites of matching projection neurons in the glomeruli. Olfactory axons also send a collateral branch across the midline into the contralateral lobe. Both sensory and projection neurons are required for proper patterning of the glomeruli.

The authors initially observed that Wnt5 overexpression in olfactory sensory neurons resulted in ectopic glomeruli forming near the midline. In flies lacking Wnt5, the antennal lobes appeared to be shortened. No glomeruli were missing, but dorsomedial glomeruli were displaced ventrally. The sensory axon branches that normally cross the midline were unable to do so and adopted an aberrant dorsal ipsilateral path. As often happens with fly mutants, the phenotype varied substantially from animal to animal. The photo shows a Wnt5-null pupa showing a relatively mild case. The antennae, with green GFP expressed in olfactory sensory neurons, are at the bottom. The olfactory axons in a double-S curve project to the antennal lobes, which appear yellow because of red counterstaining for Bruchpilot, a synaptic protein that labels all neuropil. In this individual, many olfactory axons do cross the midline, forming a thick commissure between the antennal lobes. Misrouted olfactory axon branches are nevertheless apparent, extending dorsally and ipsilaterally from the antennal lobes straight across the fly brain at the top center.

Wnt5 is a secreted protein that interacts with receptors of the Frizzled and Ryk/Derailed families to exert pleiotropic effects, including axon repulsion, in other systems. The authors show that Wnt5 in olfactory axons is required for proper development of the antennal lobes. How could its absence cause axon misrouting? Yao *et al.* propose an indirect mechanism, in which Wnt5 secreted from the axons directs crucial aspects of antennal lobe maturation. Looking for the target of axonal Wnt5, the authors report that Derailed (Drl) is strongly expressed in the projection neurons as well as in midline glia. Flies lacking Drl showed a disrupted antennae phenotype that was, in some aspects, such as ectopic glomeruli at the midline, reminiscent of Wnt5 overexpression. Selectively expressing Drl in the null mutant's glia rescued antennal morphology. Furthermore, the intracellular domain of glial Drl was not required for it to fulfill its role in antennal patterning, whereas the extracellular domain was essential. Together with the fact that either too much Wnt5 or a lack of Drl causes the appearance of ectopic glomeruli, these findings suggest that glial Drl antagonizes Wnt5 action at the midline, perhaps by binding Wnt5 and thereby limiting its activation of another, as-yet unidentified receptor. Such midline modulation of Wnt5 signaling, through further unknown steps, could affect both midline crossing of sensory axon branches and the exclusion of glomeruli from the midline.

Annette Markus