three of the operations outlined above. Short-term memory mechanisms within prefrontal cortex may automatically modulate representations of local context in other cortical regions, as has been observed in echoic memory research. This short-term memory mechanism may then signal deviations from these patterns, providing a feedback signal to prefrontal regions to view a deviance as potentially biologically significant and deserving of additional inspection. Such representations may also be accessible for systems involved in the explicit monitoring of behavior and generation of hypotheses. Evidence from neuroimaging, neuropsychology and electrophysiology supports a role of prefrontal regions in all these cognitive operations[3,8,9].

The current work can be compared to more traditional studies of pattern recognition. One approach has involved trial-and-error learning, in which participants are explicitly instructed to try to learn a response sequence[10,11]. Another has used the serial reaction-time (SRT) task, in which participants make speeded responses to successive stimuli that vary along a dimension such as spatial position or color. The SRT task is similar to that of Huettel *et al.*[1], except that the number of stimulus–response alternatives is increased, and comparisons are made between blocks of trials in which the events follow a fixed sequence or occur randomly[12,13]. This task has been used to study both explicit and implicit learning. In the former condition, participants are either taught the sequence in advance or extract it over the course of the experiment. In the latter, a distractor task is interleaved with the button-pressing task to distract the participant's attention and thus reduce awareness of the sequential nature of events.

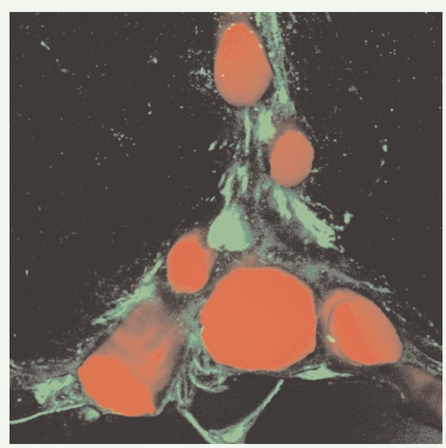
These studies have yielded a consistent picture regarding prefrontal activation during sequence learning. When learning is explicitly guided, or when participants become aware of the sequence, prominent activation is observed in prefrontal cortex, including the areas identified by Huettel *et al.* In contrast, when learning is implicit, no changes are found in lateral prefrontal cortex, even though performance measures clearly indicate that the participants have learned the sequence of stimuli and/or responses. Under such conditions, pattern recognition occurs without hypothesis generation. Thus, the sequence-learning literature is consistent with the claims of Huettel *et al.*[1] regarding a role for prefrontal cortex in the perception (or production) of patterns, but also suggests that this role may be limited to situations in which the participants are able to explicitly express these expectations.

Future work in which the level of the participants awareness is monitored should provide a direct test of this hypothesis. We would expect a marked reduction of the prefrontal response in the current task if the participants were engaged in a distractor task that disrupted their ability to generate hypotheses. "An idle mind is the Devil's workshop," goes an old English proverb. For the gambler impressed by the run of black spots in roulette, an idle mind may result in unwarranted predictions that can lead to misguided actions.


1. Huettel, S. A., Mack, P. B. & McCarthy, G. *Nat. Neurosci.* **5**, 485–490 (2002).
2. Nataanen, R. *et al. Trends Neurosci.* **24**, 283–288 (2001).
3. Alain, C., Woods, D. L. & Knight, R. T. *Brain Res.* **812**, 23–37 (1998).
4. Barcelo, P, Suwazono, S. & Knight, R. T. *Nat. Neurosci.* **3**, 399–403 (2000).
5. Miller, E. K. & Cohen, J. D. *Annu. Rev. Neurosci.* **24**, 167–202 (2001).
6. Corchs, S. & Deco, G. *Cereb. Cortex* **12**, 339–348 (2002)
7. Escera, C. *et al. J. Cogn. Neurosci.* **10**, 590–604 (1998).
8. Knight, R. T. & Scabini, D. *J. Clin. Neurophysiol.* **15**, 3–13 (1998).
9. D'Esposito, M. *et al. Brain Cognit.* **41**, 66–86 (1999)
10. Jenkins, I. H. *et al. J. Neurosci.* **14**, 3775–3790 (1994).
11. Ghiladri, M.-F. *et al. Brain Res.* **871**, 127–145 (2000).
12. Grafton, S. T., Hazeltine, E. & Ivry, R. B. *J. Cogn. Neurosci.* **7**, 497–510 (1995).
13. Hazeltine, E., Grafton, S. T. & Ivry, R. B. *Brain* **120**, 123–140 (1997).




# Putative chemoreceptors get close to arteries



Serotonergic raphe neurons within the medulla control respiratory and autonomic function. *In vitro*, these neurons can act as chemoreceptors, detecting small changes in $CO_2$ and pH in the physiological range. In support of this proposed sensing role, George Richerson and colleagues report on page 401 of this issue that the processes of these neurons are closely apposed to arterial blood vessels. Thus, these processes are in a prime location to monitor the effectiveness of lung ventilation in the blood. Because sudden infant death syndrome has been attributed to an inability to counteract rises in blood $CO_2$ during sleep with an appropriate respiratory response mediated by serotonergic pathways, these results support the suggestion that the syndrome may result from a developmental abnormality in serotonergic chemoreceptive neurons.

Using confocal imaging and electron microscopy, the authors examined the relationship between serotonergic neurons (green) and arterial blood vessels (red). Processes of the neurons were closely associated with the arterial vessel walls, in some cases less than one micron from the blood-containing lumen. Electrophysiological recordings confirmed that the serotonergic neurons in close proximity to arteries responded to changes in pH, an indirect measure of $CO_2$ concentration. The chemosensitive neurons were most common throughout the midline of the medulla, which contains large arteries and few veins. Thus the local $CO_2$ concentration in this region probably reflects arterial $CO_2$ concentration that is relatively unaffected by local tissue metabolism.

*Brian Fiske*