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Closing the Doors of Perception

ANESTHESIOLOGY is a discipline that is uniquely placed to contribute to the preeminent scientific quest of this century–namely the understanding of the neurologic mechanisms that underpin the phenomena of consciousness. The operating room is the crucible in which any putative theory should be tested. While acknowledging that there are arguments as to whether rapid eye movement sleep is really a conscious state, a simple practical approach to the definition of consciousness would include the idea of perception of the outside world. Perception involves some sort of convolution of external sensory input with the internal state of the brain. In this issue of the ANESTHESIOLOGY, an article by Hudetz *et al.* describes an ostensibly simple experiment in which they stimulated rats with flashes of light and measured how desflurane modified the resultant patterns of electrical response in the visual cortex.[1] The authors used extracellular electrodes to measure the rate of firing of neuronal action potentials (for reasons of methodological purity, the authors use the term units rather than neurons). Consonant with previous studies, they showed that increasing concentrations of desflurane reduced the unstimulated background neuronal activity. However there were more specific effects on the flash-evoked activity. Desflurane had little effect on the early neuronal responses (within 100 ms of the light stimulus) in the primary visual cortex. In contrast, the late activity (100 ms to 2,000 ms) was progressively and profoundly depressed with increasing concentrations of the anesthetic vapor. These results imply that volatile anesthetics do not inhibit the raw sensory stimulus from getting directly to the cortex, but rather profoundly inhibit the ability of the cortex to respond to and perceive this stimulus. In the presence of more than 0.7 minimum alveolar concentration of desflurane, the cortical effects of the visual stimuli simply die out and are gone after 100 ms. During general anesthesia, the rat cortex receives the input, but it is not able to integrate the information into any sort of primitive rodent cognition—*i.e.*, to say to itself: "A flash of light! Perhaps I'd better run for cover . . ."

This study contributes to a new wave of ideas and experiments that are looking at the nuts and bolts of the neuronal processes required for perception. Many of these ideas have been summarized in a detailed yet readable article by Alkire *et al.* published in *Science*.[2] From this literature, I will briefly mention two experiments that provide support for Hudetz's results. In awake epileptic patients, Quian Quiroga *et al.* recorded action potentials from the neurons in the hippocampus and medial temporal lobe in response to the patients seeing various pictures of things and well-known people.[3] They found patterns of transient activation in neuronal firing that looked very similar in time course (starting at about 200 ms and lasting up to 2,000 ms) to the delayed baseline patterns reported in Hudetz's article. In Quian Quiroga's study, the activations were achieved by more subtle cognitive events—the most famous being the neuronal "recognition" of pictures of the movie and television personality Jennifer Aniston. It appears that this subset of neurons was encoding an abstract representation of Jennifer Aniston because the neurons could be activated either by a number of entirely different pictures of Jennifer Aniston or even by a slide with no picture at all but only the words "Jennifer Aniston." Also, these neurons were not activated by pictures of other subjects, not even other young blond women. By various statistical arguments, it can be assumed that perception required activation of around 0.2% of the total number of neurons in the medial temporal lobe.[4] This implies the existence of a subnetwork of neurons (analogous to the so-called Hebbian neuronal assembly) that–given the right context–dance together in response to the Jennifer Aniston stimulus. Unfortunately, these investigators did not report on how this activation of the Jennifer Aniston neurons might have been obtunded during induction of general anesthesia for subsequent epilepsy surgery. However, I suspect that we would have seen ablation of firing patterns very similar to that reported in Hudetz's current study.

The second study pertains to the question of whether the long-distance spread of information across the cortex is inhibited by sleep and general anesthesia. Using a completely undifferentiated direct stimulus (transcranial magnetic stimulation) Massimini *et al.* stimulated a section of the premotor parietal cortex and measured the resultant spread of cortical electrical activity.[5] In agreement with numerous functional magnetic resonance imaging studies, they showed that the spread of evoked activity in the awake state was widespread in space (moving in a stereotypical sequence over most of the cortex) and prolonged in time. In contrast, the initial activation was more intense during slow wave sleep, but it then failed to spread further in space and died out quickly in time (approximately 100 ms). Similar experiments in patients under general anesthesia are underway, and a patent has been taken out–presumably with the view to developing another monitor of anesthesia. Therefore, a plausible interpretation of the observations of Hudetz *et al.* is that the delayed neuronal activation that they observed is actually a mani-

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festation of the formation of widespread assemblies of active neurons that are subsequently inhibited by the increasing concentrations of desflurane. With apologies to William Blake (1757–1827), visionary, poet, and painter, and to Aldous Huxley (1894–1963), English writer and intellectual, we may say that the desflurane is closing (and locking and bolting) the doors of perception in the cortex.

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