Not Every Stimulus Leaves an Impression

Say, why don’t I ever get any vegetables here?” The patient sounded a bit annoyed during the daily ward round, three days after he had been transferred from intensive care to a regular ward. The doctors looked at each other in surprise. It seemed that the severe stroke had done more damage to the right brain hemisphere than they had initially thought: during the three days since the patient was able to eat solid food again, he certainly had been given vegetables.

Apparently the patient’s stroke had affected not only the brain regions that control motor functions, but also regions that are responsible for complex perception processes,” says Ralf Galuske, one of the neurologists who many years ago had been involved in the treatment of the patient who complained about missing peas and carrots. Today, Galuske heads a research group at the Max Planck Institute for Brain Research in Frankfurt am Main. As is common with hospital food trays, the vegetables had been in a separate compartment on the left side of the plate. Due to the failure of a higher area in the visual cortex, the man was not able to direct his attention to the missing food on his own. Only if the plate had been turned around would his lunch have been complete for him.

Seeing something but not perceiving it is a strange concept. For most people, seeing and perceiving are one and the same. Even brain researcher Galuske has difficulty explaining the difference. That may be further proof of just how much people depend on the sense of vision. It is similar to an everyday situation that we have all encountered at one time or another: you are looking for the salt in the kitchen and dig through all of the spice containers because you suspect that the salt shaker must be somewhere behind them. And you completely miss that it had been right in front of you (where you didn’t expect it).

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Feedback from Higher Regions

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the primary visual areas can’t differentiate between the two alternative perceptions. The optical illusion of the upward-moving, lattice fence occurs only in the complete image. The neurons in the primary cortex see only a very small area of the entire whole picture and are thus confronted with the same contours in both cases. Nevertheless, we did find distinct activity patterns in the primary visual areas,” says Galuske. So something must have combined the individual stimuli in such a way that another overall impression emerges. “We suspected that these differences are caused by the feedback from the upper centers of the visual cortex. They house neurons that can integrate signals across very large areas of the visual field.”

The researchers exploit the fact that hemoglobin with and without oxygen absorbs red light differently. When the blood pigment has delivered its oxygen load to the cell, the blood absorbs far more red light than fresh, oxygen-rich blood. That is why regions in which nerve cells work hard and have greedily absorbed oxygen from the blood appear darker on the map than those where neurons are taking a break. But Galuske and his colleagues have even more than that. Neurons don’t simply fire because something happens in front of the eye – a great deal of information has to be processed by the brain first. “We don’t record the activity of the nerve cells directly, but rather indirectly,” says the scientist. Working nerve cells require oxygen. It is transported to them – bound to the blood pigment hemoglobin – through tiny blood vessels. The researchers watch the activity of the cells in area 18 with a small camera through a window – measuring about two centimeters in diameter and covered with a glass plate – in the bone above the relevant region of the cerebral cortex. The researchers exploit the fact that hemoglobin with and without oxygen absorbs red light differently. When the blood pigment has delivered its oxygen load to the cell, the blood absorbs far more red light than fresh, oxygen-rich blood. That is why regions in which nerve cells work hard and have greedily absorbed oxygen from the blood appear darker on the map than those where neurons are taking a break.
The PMLS is an area in the cortex that specializes in processing motion information. Deactivating this area has consequences for the representations and the neuronal activity in area 18: the color-coded direction maps (a) show that the allocation of the various direction-selective regions changes significantly during PMLS deactivation (center). The white crosses in the maps mark the same locations in each case; the assignment of the various colors to the different motion directions is pictured at the outside right. (b) The dot clouds reveal that the cooling causes individual regions of area 18 to change their preference for certain directions of movement. That is far more than simply turning the volume knob up and down, and much rather as if a rock fan had given an axis preferences and now also listens to Handel. "The feedback makes a true qualitative difference," says the scientist.

Knowledge Changes How We See the World

But optical examination under red light allows conclusions to be made only about entire populations of neurons. Electrophysiological recording with superfine wires is required to study individual neurons. And this shows that the feedback influences primarily those neurons in area 18 that are particularly direction-sensitive, while the other neurons that aren’t as selective are far less responsive to the feedback. "Feedback not only regulates the general intensity of the response, it controls very specific groups of neurons," says Ralf Galuske. Even in the very early processing steps, the knowledge of the higher centers systematically changes our view of the world, as it were, and so appears to dictate, or at least facilitate, our interpretations.

The feedback can also help explain why we sometimes see things that aren’t there at all – like the optical illusion of the moving lattice fence. And at the same time, it can explain why we sometimes don’t see things even though they are right in front of our nose – like the salt shaker in the front row.

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Depending on just what the neurobiologists are examining, they analyze the reactions to different stimuli in that part of the visual cortex in various maps – which are second to none among the great masterpieces of abstract painting. Black-and-white patterns visualize activity or a certain stimulus preference, while colorful superimpositions serve, for example, to recognize directional preferences across the entire region.

Thus, different color or black-and-white patterns show how the visual cortex processes the images when the cat watches a three-second television program with horizontal grating patterns, clouds of dots drifting to the right or left, or layers of gratings sliding on top of each other. All of this serves a single purpose: to find out what influence feedback from the higher visual centers PMLS and PLLS has on the lower-lying regions in the primary visual cortex, such as area 18. But to eliminate this influence, one would have to observe area 18 and, at the same time, be able to switch the feedback on and off. And that is precisely what Ralf Galuske and his team managed to do.

The most direct method would be a lesion – that is, the removal of part of the nerve tissue. "That is very drastic, because the brain is highly traumatized afterwards," says Galuske. One would have to wait awhile until the brain has recovered. If one waits too long, then it’s possible that the functions of the relevant region of the brain would have been taken over by another, and the malfunction thus already compensated for. "Then you see only the compensated state."

Nerve Cells Put into an ICY Sleep

Another option would be pharmacological intervention. There are numerous substances that inhibit the activity of neurons and stop neuronal processes locally. However, it is very difficult to employ these drugs so extensively that they block the activity of an entire cortical area," says Ralf Galuske. The amounts required could then exhibit undesirable effects at many other locations in the brain.

Bertram Payne and Stephen Lomber, two American colleagues from Boston University with whom the group in Frankfurt collaborates, supplied a technique that avoids these problems. "We do it thermally," says Galuske. The researchers transferred the cortical area into a kind of hibernation for a short time. Freezing-cold methanol flows through a thin metal tube that is bow-shaped at the end. When it comes out of the dry ice, it has a temperature of minus 70 degrees Celsius.

In this way, the tissue is chilled to 3 to 5 degrees, and to 10 degrees in somewhat lower layers. "That is enough to hinder nerve cells from generating any more action potentials." The result is a neglect – as in the patient who overlooked his vegetables. In lab tests, the cat, too, then no longer perceived snacks on one side, although it had previously eaten them. When the researchers stop the cooling, the brain area recovers within minutes and again fires action potentials.

The comparison of the maps and data with and without neglect initially confirms what some researchers had already suspected: there are simple quantitative differences. Without feedback from the upper levels, the overall activity in area 18 drops. The maps appear pale where there had previously been strong black-and-white contrasts. "If that was the only thing that happened, it wouldn’t be particularly exciting. The feedback would merely have a gain-setting function," explains Galuske. It would be nothing more than an amplifier in a stereo system, and the neglect would have an effect comparable to a turned-down volume knob.

But there is more happening: when the feedback is turned off, the activity patterns corresponding to the global perception of the fence no longer appear on the maps. Only the individual components of this complex stimulus are shown. Really exciting are the directional preferences. The dot clouds reveal that the cooling causes individual regions of area 18 to change their preference for certain directions of movement. That is far more than simply turning the volume knob up and down, and much rather as if a rock fan had given an axis preferences and now also listens to Handel. "The feedback makes a true qualitative difference," says the scientist.