A new primary visual cortex
The postrhinal cortex joins V1 as a first-order processor of visual information

By Riccardo Beltramo

In the mid-19th century, Bartolomeo Panizza, a professor at the University of Pavia, observed patients who became blind after a stroke in the posterior part of their brain and made a bold claim: Visual function is localized in the cerebral cortex (1). Given that widely accepted theories at that time assumed that all parts of the brain equally contributed to every mental activity, the idea of localized function—a fundamental pillar of modern neuroscience—was truly revolutionary. Performing targeted cortical ablations in animals, Panizza confirmed his hypothesis of a cortical region dedicated to visual processing, which became known as the primary visual cortex, or V1.

V1 receives retinal input through the dorsolateral geniculate nucleus of the thalamus and extracts basic features from the visual world (2). It then projects to a constellation of higher visual cortices that compute more complex aspects of the visual scene (2). The classical hierarchical model of cortical processing implies that visual responses in downstream areas depend on the activity of V1 (3). Indeed, in multiple species, from cats to rodents to primates, lesions of V1 severely impair the visual responses of all known higher visual cortices (3–7). Thus, V1 has long been considered the driver of all visually evoked activity in the cortex.

AN UNCONVENTIONAL PRIMARY VISUAL CORTEX
Panizza’s pioneering studies and our mutual Italian ancestry inspired my postdoctoral research. I began by characterizing the anatomy, function, and gene expression of V1 cells in the mouse visual cortex, focusing on V1 neurons that target higher visual cortices (8). Fascinated by the hierarchical organization of the cortex (3), I wanted to determine whether visual responses in downstream visual areas depend on V1 activity, as posited by traditional dogma.

Taking advantage of the optogenetic tools available for use in mice, I systematically verified the effects of silencing V1 on the responses of downstream visual cortices (9). I discovered that one of them—the postrhinal cortex (POR)—was minimally affected upon V1 silencing. The POR is a lateral-temporal cortex (10) known to be innervated by V1 axons (11). If this region does not receive visual input from V1, I wondered, where does this information come from?

The dorsolateral geniculate nucleus relays retinal information to V1 and also projects to higher visual cortices (12). To test whether the POR receives direct geniculate input, I injected it with retrograde tracers. I found that the POR did not receive geniculate afferents but was heavily targeted by another thalamic nucleus: the caudal pulvinar. But which structure relayed visual information to the caudal pulvinar and POR?

A ROLE FOR THE SUPERIOR COLLICULUS
In 2019, less than 100 miles from the laboratory where Panizza discovered V1, an Italian neurophysiologist at the University of Turin received a threatening letter. Enclosed inside was a bullet. The researcher, neuroscientist Marco Tamietto, had been targeted by animal rights activists for experiments involving V1 microlesions in primates (13). His studies focused on an enigmatic condition referred to as “blindsight” (14).

Blind sighted patients are clinically blind from V1 lesions. However, they still respond to moving stimuli without consciously perceiving them. This intriguing phenomenon is believed to depend on a phylogenetically ancient structure called the superior colliculus (SC) (15). The SC, which is also found in nonmammalian vertebrates, receives direct input from the eye and projects to the caudal pulvinar (16). Could this ancestral structure drive the visual processing of the POR?

Using anterograde transsynaptic viral tracers (17), I established a disynaptic connection between the SC and the POR and found that the caudal pulvinar neurons targeted by collicular axons directly innervate the POR.

But is this the route taken by visual signals to activate the POR independently of V1? I needed functional evidence to answer...
Left: Schematic of the anterograde transsynaptic tracing experiment. An anterograde transsynaptic virus harboring Cre recombinase was injected in the superior colliculus. A Cre-dependent green fluorescent protein (GFP) reporter was injected into the caudal pulvinar, which labeled in green the thalamic neurons receiving collicular afferents. A td-Tomato reporter was injected into V1, which labeled in red the V1 axons targeting the POR. Middle: Transsynaptically labeled neurons (GFP, green) targeted by collicular axons. Dotted line: Boundaries of the caudal pulvinar. Right: Double labeling of axons targeting the POR. Red, V1 afferents; green, caudal pulvinar afferents. Inset: Magnification of the region marked by the square.

this question. I optogenetically and pharmacologically silenced the SC to determine whether this perturbation would affect the POR's response to visual stimuli. Strikingly, collicular silencing abolished visual responses in the POR. My findings redefine the POR as a new cortical primary entry point for visual information independent of V1 and uncover a cortical area dedicated to collicular input (9). But why are there two cortical entry points for visual information? Does the POR extract specific information that is not already captured by V1?

WHAT THE FROG’S BRAIN TELLS THE MAMMALIAN VISUAL CORTEX

Seminal experiments on amphibians (18) have shown that the SC (called “optic tectum” in nonmammals) exhibits robust responses to small moving objects; think flies crossing the visual field of a frog. This feature earned the optic tectum the name “bug-detector” (18).

If the distinctive collicular response properties are transferred to the POR, I reasoned, neurons in this region should detect small moving objects, perhaps even better than V1 neurons. To test this hypothesis, I recorded POR and V1 responses to small moving stimuli presented to head-fixed mice. POR neurons significantly outperformed V1 cells in distinguishing the linear motion of small objects.

What is the use of such neurons? Perhaps the POR's exquisite sensitivity to motion facilitates the detection of movement while V1 facilitates the discrimination of the nature of the moving object, telling us, for example, whether it is a beautiful butterfly or a dangerous hornet. The POR might also be involved in blindsight because blindsighted people maintain visual responses to moving stimuli in lateral-temporal cortices (19), where the POR resides.

Almost two centuries after Panizza’s discovery, my findings demonstrate the existence of another primary visual cortex. Evolutionary anatomists have theorized that in a hypothetical ancestral vertebrate, the collicular pathway was the original link connecting the eye to the cortex, before the geniculate-V1 pathway development (20). If that is indeed the case, it is tempting to regard the POR as our ancestral primary visual cortex.

REFERENCES AND NOTES

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