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Neural coding: Stimulating cortex to alter visual perception

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A new study has shown that monkeys detect transient external pulses delivered to the highest echelons of visual cortex in a way that depends on concomitant visual inputs. This new work, a technical *tour de force*, has implications for the development of future visual prosthetic devices.

It is tempting to assume that what we perceive is a veridical reflection of what is out there in the world as captured by our senses. However, a plethora of visual illusions and neuroscience experiments show otherwise. Brains make up stuff. In an elegant and courageous experiment, reported recently in *Current Biology*, Azadi, Bohn *et al.*[1] show that monkeys can detect external activation of small patches of high visual cortical areas, and that what they perceive depends on a combination of the external stimulation with the concurrent patterns of inputs to their eyes.

Perception is a construct enacted by the activation patterns of neurons in the cortex. Therefore, it stands to reason that if we could tickle, that is, activate, neurons in the visual cortex, we would be able to see things. Indeed, injecting electrical stimulation into the primary visual cortex leads to the perception of brief flashes of light in a topographically-specific fashion consistent with our understanding of the neuroanatomy and neurophysiology of the visual cortex[2,3]. Beyond the primary visual cortex, the situation has been far more complicated. Several studies have demonstrated that electrical stimulation can bias recognition of ongoing stimuli, for example, by enhancing motion reports in a specific direction[4] or enhancing face discrimination reports in a specific way[5]. Beyond intriguing anecdotal examples[6], however, creating complex visual percepts by electrical stimulation with eyes closed has remained elusive.

As a rough analogy, imagine an orchestra of talented musicians (the neurons). If one were to force many musicians to execute some random movement on their instrument (in the case of neurons, stimulating them to emit spikes), it is a safe bet to assume that nothing too lyrical would come out: listeners (or post-synaptic neurons) would not be able to interpret such sounds, which would be entirely unlike anything they had heard before, especially given the background noise. Creating music by pushing the members of an orchestra to tap their instruments randomly seems highly unlikely. But this is *not* what Azadi, Bohn *et al.*[1] set out to accomplish. Instead, the authors reasoned that it would be easier and more revealing to let the musicians play their own songs and then insert minor variations on the theme. They let the orchestra play a beautiful piece — by presenting images to the retina, eliciting natural neuronal responses — and subtly manipulated a small number of musicians (neurons), a relatively small subset compared to the whole orchestra. In this case, the attentive listener can readily appreciate the injected changes, and detectability depends on which partiture is being played.

Instead of traditional electrical stimulation methods, Azadi, Bohn *et al.*[1] used a state-of-the-art technique known as optogenetics[7]. In a nutshell, optogenetics involves inserting a light-sensitive protein into neurons such that shining light on the tissue will activate those neurons — or inactivate them, depending on the type of light-sensitive molecule used. This technique is reversible, spatially and temporally localized, and gives unprecedented control over neural circuits. The authors used such an optogenetic method to transiently excite monkey neurons in an area of the inferior temporal cortex responsible for visual object recognition[8].

Macaque monkeys were trained to report their sensing of optogenetic pulses. Monkeys found it challenging to discern optogenetic stimulation when their neurons were activated while viewing a blank screen (like creating music by random taps on instruments). In contrast, monkeys were highly proficient in noting whether their neurons were optogenetically tickled whenever pictures were simultaneously presented on a

monitor. The ability to detect optogenetic pulses depended on the neural stimulation site; modulating the violins is different from altering the flutes in our analogy. Similarly, pulse detection was modulated by the contents of what was shown on the monitor (altering violins may be more critical with a Vivaldi piece for strings than a Dvořák piece for wind instruments). Detection was also strongly affected by the intensity of optogenetic stimulation (perhaps analogous to how many musicians alter their playing). Future work will reveal how the natural activation patterns of neuronal ensembles interact with the effects of optogenetic stimulation and perhaps lead to quantitative models that enable 'playing the cortical piano'[9] and thus create novel percepts. These exciting results shed further light on the complex relationships between neuronal activities and perception.

Beyond the elegance of the experiments and their impact on our understanding of neural coding, Azadi, Bohn *et al.*[1] argue that these results could have exciting implications for the development of prosthetic applications. The observations suggest that it is challenging to elicit complex visual percepts by stimulating the higher visual cortex in blind individuals unless we have methods to orchestrate precise neuronal activation patterns. This situation is approximately equivalent to the blank screen condition in the monkeys. The results also suggest that there may be potentially rewarding paths to combine direct neuronal stimulation with concomitant visual input in subjects with visual impairment. And perhaps in the long-term future, this study also hints at initial steps towards thinking about the tantalizing opportunities of augmenting cognition via direct neuronal stimulation.

DECLARATION OF INTERESTS

The author declares no competing interests.

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Mitosis: Augmin-based bridges keep kinetochores in line

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A recent study highlights the indispensability of the augmin complex for the construction of mitotic spindle bridging fibers, which in turn support accurate chromosome attachment and segregation.

The mitotic spindle is a critical piece of cellular machinery whose job is to deliver exactly one copy of each chromosome to each new daughter nucleus during cell division. To accomplish this function, the spindle builds itself from scratch each time the cell divides. An analogy with macroscopic structures can help elucidate the magnitude of this task (Figure 1A). If we consider large human-built structures, such as a skyscraper or a suspension bridge, they often contain many similar parts (I-beams, bolts and nuts, etc.) despite having very different organizations. Similarly, the spindle reuses many of the components from the interphase cytoskeleton (most notably, microtubules and some of the proteins that bind them). However, unlike a skyscraper or a suspension bridge, the spindle assembles without a construction manager to coordinate its activities. How does the spindle machinery self-organize without a master planner? A central tool in this feat is local biochemical feedback loops that are then reinforced within global scale structure. Results from Štimac and colleagues that were recently published in *eLife*[1] describe a new example of this pattern within the mitotic