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Visual Neurophysiology: Recordings from the Human Primate

Dispatch

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Neurophysiological studies in human patients, with experiments of the kind traditionally reserved for monkeys, are beginning to provide valuable insight into the workings of the brain. Taking center stage is the question of which neurons lie at the heart of perception itself.

Why do neuroscientists study the brain? It must be conceded by even the starkest reductionist that our fascination with the brain arises first and foremost from a curiosity about ourselves. This is particularly true regarding our perceptual experience — we cannot fathom how a biological machine, regardless of how complicated, can fashion our own subjective impression of the world. For primates, including humans, this impression is shaped primarily by sight. It is therefore perhaps unsurprising that visual perception has been the topic of studious research from the time of the ancient philosophers to the present [1,2]. Physiological inquiry into the brain, by comparison, is in its infancy. Only in the last decades have microelectrode recordings in monkeys revealed the wealth of areas in the primate brain dedicated to the analysis of the visual world [3]. In these areas, single-cell recordings have disclosed a systematic and highly parallel strategy for registering and interpreting light patterns that enter the eye [4,5]. But in spite of a growing knowledge base of cortical subdivisions and neural response predilections, many would argue that we lack a fundamental understanding of the brain's approach to vision, including the mysterious nature of subjective perception.

In recent attempts to address the neural basis of perception, some animal studies have compared patterns of single-cell activity directly to perceptual experience [6,7]. Such experiments have generally relied upon trained monkeys to make judgments about visual patterns that are either inherently ambiguous or at the edge of their perceptual abilities. By matching up neural responses with the reported subjective experience on a trial-by-trial basis, the role of individual neurons in perception can be addressed. Interestingly, many experiments suggest that activity in the visual cortex is not simply a re-representation of the original retinal image, but instead reflects some aspects of how that image is actively interpreted — what psychologists call perceptual organization. Moreover, neurons carrying perception-related signals appear to be neatly interwoven with those whose responses can best be described as purely sensory, making the link between neural firing and subjective perception that much more complex.

This combined behavioral/electrophysiological approach has been invaluable, but unfortunately it is limited by the cognitive boundary inherent in communication between monkey and man (Figure 1). For example, with a fair amount of training, a monkey can respond to the question "Did you see A or B?", but never to the question "What exactly did you see?" In the last few years, human subjects have played an increasingly prominent role in the investigation of brain mechanisms of perception, largely because of the advent of functional magnetic resonance imaging (fMRI) [8]. But while the use of humans has provided flexibility in the types of cognitive task that can be investigated, the fMRI technique is currently limited in its spatial and temporal resolution, making direct comparison with single unit data difficult.

Recent developments in human electrophysiological recordings have added a promising new dimension to the investigation of the visual brain. In particular, a series of studies led by neurosurgeon Itzhak Fried and colleagues [9–12] has systematically examined the activity of single, isolated neurons that appear to be closely linked with perception (Figure 2). They recorded neural impulses from electrodes implanted deep within a part of the brain known as the medial temporal lobe (MTL). This region, which includes a portion of the cerebral cortex, as well as the phylogenetically older amygdala and hippocampus, is thought to be critical for visuocognitive function, as bilateral damage can lead to significant impairment in the memory for objects and events [13].

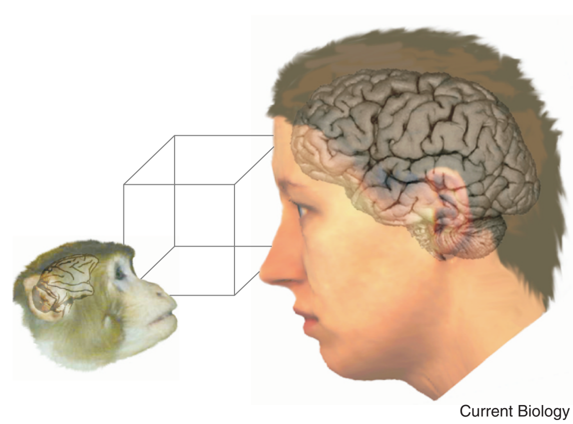

Figure 1.

Neurophysiological studies of visual perception have traditionally relied upon monkeys trained to report their perceptual experience. Microelectrode recordings in human patients are now beginning to address similar questions. While fraught with practical obstacles, these experiments have the potential to tap into aspects of our perceptual experience that are inaccessible with the nonhuman primate.

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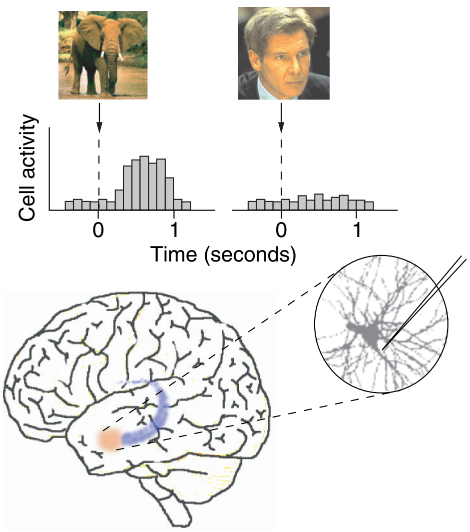

	Category A *Animals*	Category B *Faces*
Normal presentation *Presented and perceived*	+	-
Visual imagery *Not presented but imagined*	+	-
Flash suppression *Presented and perceived*	+	-
Flash suppression *Presented but not perceived*	-	-

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Figure 2. Single neurons recorded from deep within the human brain reveal category-specific responses to visual stimuli.

In this example, a neuron in the amygdala responded to pictures of animals, but not to other categories such as faces. Testing with diverse perceptual paradigms demonstrated that the responses of such neurons are closely linked to the patients' subjective perception of the stimulus. For example, a neuron that responds selectively to animal photos might also respond when an animal is imagined, but not when a face is imagined. Similarly, in the phenomenon of flash suppression, an excitatory stimulus fails to give a response if it is not subjectively perceived. Key: +, excitatory neuronal response; –, no neural response.

Fried and colleagues [11] previously discovered, not only that that neurons in these areas respond to a variety of visual stimuli, such as faces, animals and spatial layouts, but also that the response of many of the neurons adhered strictly to high-level categorical boundaries. The same group then showed that selective neural responses could, remarkably, be elicited even in the absence of a visual stimulus if the patient was instructed to conjure up a subjective impression of a previously seen photograph using mental imagery [10].

Microelectrode recordings from the human brain have a long but sparse history, and have come almost exclusively from the need to localize seizure foci in epileptic patients [14]. These experiments are challenging, requiring the use of sophisticated electrophysiological techniques in a most inconvenient and often unwelcoming hospital setting. The testing time is extremely limited, and possible only through the generous consent of the patients themselves. Yet despite these obstacles, Fried and colleagues have been able to bring human recordings to a systematic level that is directly comparable to studies in monkeys.

In their most recent experiment, for example, Kreiman *et al.* [12]. examined the firing of MTL neurons to patterns that were physically present, but perceptually invisible because of a visual trick called 'flash suppression'. Flash suppression is closely related to the well-studied phenomenon of binocular rivalry, where dissimilar patterns, presented separately to the two eyes, alternate in their perceptual dominance [15]. Like rivalry, flash suppression is a paradigm in which a single sensory pattern gives rise to two distinctly different percepts, and it can therefore be used to differentiate between sensory-related and perception-related neural signals [16]. With the patients sporting stereoscopic glasses, Kreiman *et al.* [12] presented one visual pattern to one eye, followed after a short delay by a different pattern to the other eye, while the first pattern remained present. Previous work has shown that such manipulations consistently result in the sustained perception of the latter pattern and complete perceptual suppression of the former, despite the physical presence of both stimuli [17].

Kreiman *et al.* [12] found that the activity of most visual neurons throughout the MTL depended squarely on the patients' subjective percept — never would a neuron respond to a pattern that was perceptually invisible. These results are directly comparable to those from an earlier electrophysiological study in monkeys by Sheinberg and Logothetis [18]. In their experiments, they also used flash suppression to bias perceptual dominance, and recorded from neurons in the inferotemporal cortex, an area with direct inputs to the MTL. Just as in the new human study, nearly all recorded neurons responded to an excitatory stimulus if and only if it was reported to be visible by the monkey.

The results of Kreiman *et al.* [12] are important for at least two reasons. First, they suggest that visually responsive neurons in the MTL directly correlate with phenomenal visual experience, thus providing an additional data point for our growing understanding of how neural activity contributes to subjective perception [19]. And, perhaps more importantly, these and a handful of other studies [14,20] demonstrate that microelectrode recordings in human patients can provide valuable additional information for interpreting experiments in monkeys. By using similar paradigms, they can be used to assess the validity and generality of conclusions drawn from animal studies. And by using techniques that are beyond the grasp of research in the non-human primate, such as visual imagery, they can forge new ground in our understanding of brain mechanisms underlying human perception and cognition.

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