Chapter IV. Creating and altering visual percepts through lesions and electrical stimulation

Supplementary contents at **http://bit.ly/3abKBpP**

We want to understand how neuronal circuits give rise to vision. We can use microelectrodes and the type of neurophysiological recordings introduced in **Chapter II**. In the case of the retina, it is evident where to place the microelectrodes to examine function. However, there are about 10^{11} neurons in the human brain, and we do not have any tools that enable us to record from all of them. How do we figure out what parts of the brain are relevant for vision so that we can study them at the neurophysiological level?

To find out how a device works, it is often useful to take it apart, inspect its elements carefully, examine the device's function upon systematically removing individual components, put the device back together, and ensure that the original function is restored. An extraterrestrial coming to Earth intrigued by how cars work might find out that the car can still navigate quite well upon removing the radio, but the car fails to start without the battery.

Trying to figure out how the brain works by examining the behavioral consequences of restricted lesions has been a fundamental approach in Neuroscience since the very beginnings. The history of brain science can be traced back to the famous Edwin Smith Surgical Papyrus, which dates back to the 17th century BC, and which describes the symptoms of two warriors who suffered wounds in the head. Despite this early description, for centuries, people believed that the heart was the seat of cognition. The erudite philosopher Aristotle (384 – 322 BC) believed that the purpose of the brain was to cool down the blood and maintained that the heart contains the rational soul. It was again the study of head injuries, skull fractures, and spinal injuries that brought back the discussion of mental events to the brain.

Deducing the function of different brain structures by the examination of lesions is easier said than done. First, different components of the system may interact with one another to perform any one particular task, such that removing one of them could lead to indirect functional consequences beyond those directly associated with the loss of the lesioned tissue. Second, there could be a significant amount of redundancy, such that another component could take over, thereby shadowing the actual function of the lesioned area. Third, it is not particularly easy to remove specific parts of the brain. Despite these challenges, much has been learned about visual circuit function through lesions in animals and humans.

In addition to lesions, another approach to evaluate the role of specific brain areas in visually triggered behavior has been the injection of electrical

currents to manipulate brain function. Invasive brain stimulation can trigger activity in neurons within circumscribed regions and help test hypotheses about the involvement of those neurons in visual processing.

IV.1. Correlations and Causality in Neuroscience

As often stated, correlations do not imply causation (*Non Causa Pro Causa*, in Latin). This simple logical statement is often ignored, leading to much confusion and misinterpretation of cause and effect in Neuroscience, as well as in many other disciplines. There are plenty of examples of this type of misinterpretation in the news. For example, the following statements extracted from news articles can easily be misinterpreted to imply causality: "Smoking is associated with alcoholism"; "Girls who watch soap operas are more likely to show eating disorders"; "People who go to museums live longer." Whether these statements are true or not is irrelevant here. These statements reflect correlations reported by journalists, and readers might erroneously infer some form of causality. The medical community is not immune to this fallacy. Consider the following statement: "The majority of children with autism are diagnosed between the ages of 18 months and three years old. That is also the same period when children receive a large number of immunizations. People see the correlation between receiving immunizations and the diagnosis of autism, and assume that the immunizations cause autism." The correlation between the age of immunization and the appearance of autism syndromes does *not* imply any causal relationship between the two.

In the next chapters, we will examine the activity of individual neurons along visual cortex. Those neurophysiological recordings provide *correlations* between neuronal responses and visual stimuli, or *correlations* between neuronal responses and visually evoked behavior. Moving beyond these correlations to establish causality is not a trivial matter. We will consider here two approaches that can help bring us a step closer towards understanding the relationship between neural activity in specific brain circuits and visual perception: lesions and electrical stimulation.

IV.2. A panoply of lesion tools to study the functional role of brain areas in animals

Investigators take advantage of several tools to examine the effect of removing or silencing a brain area, including physical lesions, cooling experiments, pharmacological intervention, cell-specific ablation, molecular tools such as gene knock-outs, and optogenetics.

Physical lesions. One of the most widely used tools to study function in the brain has been the behavioral examination of subjects with physical lesions. It is also possible to induce lesions by injecting chemicals like neurotoxins. In non-human animals (henceforth animals), investigators may remove specific brain areas to

examine the behavioral deficits. For example, retinal ganglion cells project to primary visual cortex (via the LGN) and to the superior colliculus. Primates with lesions to the superior colliculus are still capable of solving visual recognition tasks, whereas animals with lesions to primary visual cortex are not. Subsequent studies examined the function of different parts of visual cortex through lesions. Lesions to an area known as the middle temporal area (MT, also known as area V5) lead to severe impairment in the ability to discriminate motion direction, whereas lesions to inferior temporal cortex lead to object recognition deficits.

Lesion studies in animals often provide highly valuable information, but they are not always easy to interpret. First, it is challenging to make anatomically precise lesions. Second, behavioral assessment may not be trivial: unless the animal shows a definite impairment in a battery of often pre-defined tasks, important deficits could be missed. Finally, by definition, lesions defined by anatomical landmarks impact multiple cell types and multiple connections, including inputs and fibers of passage. As a rough analogy, imagine removing the entire state of Massachusetts from the US. The loss of economic activity from Massachusetts may have effects on the broader economy that are difficult to predict, the loss of the infrastructure of major highways and rail lines that run through Massachusetts may also impact traffic and other economic activity in New England and other regions, and removing 114 colleges could impact educational opportunities. There would be severe deficits, but some may not be obvious to spot, some may not be unique to Massachusetts, some may not be immediate and may require time to appreciate, and some may require detailed insights about what to look for.

Cooling. Neuronal activity decreases sharply when the temperature of the brain or a given brain region is lowered (***Figure IV-1***). Cooling devices can be implanted in the brain to lower the local temperature by several degrees. Lowering the temperature can silence activity in the region surrounding the cooling probe. In contrast to physical lesions, cooling is a transient and reversible procedure so that the same animal can be studied before, during, and after the effects of inactivation.

*INSERT **Figure IV-1** ABOUT HERE*

***Figure IV-1. Cooling a patch of cortex can essentially abolish activity in the local circuitry**. **A**. Raster plots, showing each action potential as a dot, when a bar was swept repeatedly across the receptive field of a neuron in visual area V2 in an awake macaque monkey. Each row is one sweep lasting 1.5 seconds, and consecutive sweeps are shown from bottom to top. Arrows indicate when a pump is turned on to cool an area in the vicinity of the recording electrode, and when the pump is turned off again. Within a few minutes of turning the pump on, activity is reduced. **B**. Mean visually evoked activity (spontaneous activity subtracted) over time. Visual activity is eliminated within 4 minutes of turning the pump on. Modified from Ponce et al. 2008.*

Pharmacology. Pharmacological intervention can also be used to reversibly silence brain regions. The most well-known type of chemical intervention is

perhaps general anesthesia, where large parts of the brain are affected, and the patient is "put to sleep." It is also possible to inject neuronal inhibitors to affect activity in *local* circuits. Pharmacological silencing procedures are often reversible, and the silencing effects disappear when the drugs wash out. One of the most common forms of pharmacological intervention is the use of *muscimol*. Muscimol is a potent activator of a specific type of receptor for the brain's main inhibitory neurotransmitter, GABA. It is also one of the main psychoactive components of several types of psychedelic mushrooms. Muscimol has been extensively used to induce local silencing of neural activity. Another common example is the use of *lidocaine*, which acts by extending the inactivation of the fast voltage-gated sodium channels, leading to a reduction or elimination in the possibility of triggering action potentials.

Cell ablation. In a few heroic studies, investigators have used high-resolution imaging tools to identify specific cell types and then ablated those cells one-by-one to examine the behavioral consequences. Cell ablation is not a reversible procedure, it is difficult to inactivate large areas with this protocol, and it is a particularly challenging experiment because of the requirement to manually go through the cells to be inactivated. The effort is rewarded by a unique ability to remove individual cells from the circuit.

Gene knock-outs. To describe gene knock-outs, let us first briefly summarize the central tenets of molecular biology. Genetic information is stored in DNA. Each cell can *express* different genes along the DNA, meaning that those genes are converted into a messenger molecule called RNA, and subsequently translated into proteins. Powerful molecular biology tools allow silencing expression of specific genes through *knock-outs* and *knock-ins*. These techniques allow studying the consequences of removing specific genes, adding specific genes, or altering the timing or spatial pattern of expression of specific genes.

Furthermore, a recent technique known as *CRISPR* allows investigators to edit individual nucleotides in specific genes. These techniques can be applied in such a manner that animals are born with the modified gene expression patterns. Alternatively, these manipulations can also be programmed in an inducible format so that the changes only take effect when the investigator turns them on. Such molecular manipulations have traditionally been the domain of work in mice, and it remains difficult, though not necessarily impossible, to use these techniques in primate research. More recently, primate researchers have turned their attention to virus injection techniques that could achieve high molecular specificity without having to incur in the time and cost of developing knock-outs.

*INSERT **Figure IV-2** ABOUT HERE*

***Figure IV-2. Silencing specific neuronal populations via optogenetics**. Activity of a silenced neuron during and after 1 second of light illumination in an optogenetics experiment. Top: Action potential waveforms elicited before illumination (left), during illumination (middle), or after illumination (right); shown is the mean (black) as well as*

the overlay of raw waveforms (gray). Middle: Single neuron activity, shown as a spike raster plot, and as a histogram of instantaneous firing rate averaged across trials (bottom; bin size 20 ms). Bottom: Histogram of instantaneous firing rate, averaged across all silenced single units recorded upon 1 s green light exposure. Black line, mean; gray lines, mean ± standard error (SE); n = 45 silenced single units. Modified from Han et al. 2011.

Optogenetics. A particularly exciting and promising novel tool to silence – or activate – a specific population of neurons is *optogenetics* (***Figure IV-2***). Introduced by Ed Boyden and Karl Deisseroth, optogenetics constitutes a transformative technique to manipulate neural activity of cell types of interest with unprecedented resolution and control. Briefly, neurons are genetically modified by injecting a virus to express a light-sensitive ion channel. This ion channel is expressed only in specific neurons and not others by virtue of the *promoter* that drives its expression. The promoter is a region of DNA, typically sitting right upstream from the gene itself, which is responsible for controlling when and where a given gene will be activated. Once the neurons of interest express this light-sensitive ion channel, the cells are ready to be manipulated by shining light on the tissue. The opening of some ion channels can lead to excitation (depolarization of the neuronal membrane), whereas the opening of other ion channels can lead to inhibition (hyperpolarization of the neuronal membrane). By injecting a virus carrying an inhibitory channel, expressing that channel only in a subpopulation of neurons and shining light on the tissue, it is possible to turn off only certain types of neurons, in a temporally restricted and reversible manner.

Several distinctions need to be made while considering studies involving lesions and silencing. First, as noted above, many of the techniques like physical lesions involve removing (or silencing) large amounts of tissue. Therefore, an often-encountered discussion in the literature concerns the separation of local effects from "fibers of passage" effects. Imagine that axons going from area A to area C happen to pass near area B. A lesion to area B may also cut through the A→C axons. An investigator performing a lesion in area B may draw conclusions about the functional roles of area B. However, it may turn out that the behavioral consequences of the lesion may not be due to the function of area B at all, but instead to the function of areas A or C, whose communication was severed while removing B.

Another distinction to be made concerns immediate versus long-term effects. The brain has a remarkable degree of plasticity. Over time, the behavioral effects of lesions to a given brain area could be overcome through compensatory adjustments in other brain areas. One such potential compensatory mechanism is the presence of a "copy" of the same brain area in the other hemisphere. Many (but not all) parts of the brain have analogous counterparts in the other hemispheres. The effects of unilateral lesions (lesions in only one hemisphere) can be masked by activity in the other hemisphere (unless specific precautions are taken in the experimental design).

IV.3. Some tools to study the functional role of brain areas in humans

Due to obvious ethical reasons, most of the techniques discussed in **Section IV.2** cannot be used in studies in human subjects. There are, however, a wide variety of neurological conditions that provide important insights about functional neuroanatomy of the human brain. These cases typically come from a variety of neurological conditions, accidents, and wounds. We mentioned Oliver Sacks in **Chapter II**; he was an influential neurologist who wrote extraordinary and intimate accounts of patients visited with a wide variety of mental conditions. In the prologue to one of his books describing the consequences of lesions in the human brain, he wrote, "… feeling in part like a naturalist, examining rare forms of life, in part like an anthropologist, a neuroanthropologist, in the field … These are tales of metamorphoses, brought about by neurological chance, but metamorphoses into alternative states of being, other forms of life, no less human for being so different".

Bullets and wounds inflicted by other weapons have provided critical insights about function in visual cortex. Carbon monoxide poisoning, as well as certain viral infections such as encephalitis, often produce severe visual deficits, especially when occurring in the temporal lobe. Head trauma, partial asphyxia during the first weeks of life, tumors, and hydrocephalus (accumulation of cerebrospinal fluid), can also result in visual deficits.

To study the consequences of lesions, it is always important to design the experiments carefully. Otherwise, even remarkable behavioral deficits associated with lesions could be missed. Consider, for example, the case of split-brain patients. These are patients with pharmacologically resistant epilepsy who undergo severance of the primary fibers that connect the two hemispheres, the corpus callosum fibers, as a treatment for epilepsy. For a long time, it was assumed that there was nothing out of the ordinary with these subjects who had their two hemispheres mostly disconnected (not completely disconnected because there are a few other smaller fiber tracts that also connect the two hemispheres). It was not until Roger Sperry (1913–1994) designed careful experiments based on his scientific understanding of the neuroanatomy of the visual system that some of the deficits became apparent. Sperry knew that the right visual hemifield maps onto the left hemisphere in visual cortex and vice versa.

As described in **Chapter II**, it is essential to distinguish between the right and left *eyes* and the right and left *visual hemifields*: the right and left visual hemifields are defined by the position in a visual scene with respect to the fixation point. Thus, every time you move the eyes and fixate on a new location, the location of each hemifield changes. Most of the information from the right hemifield reaches both the left and right eyes (and most of the left hemifield reaches other parts of the retina in both the left and right eyes). By using a simple divider, Sperry designed an experiment where visual information about an

object reached only the right hemisphere (information from the left hemifield). Thus, information about the object was not accessible to the left hemisphere. Because for most right-handed people, the left hemisphere is critical for language, Sperry demonstrated that the subjects were unable to name the objects. Conversely, when object information reached only the left hemisphere, subjects had no problem in naming the objects. Sperry was awarded the Nobel Prize for this work in 1981. Previous studies in these subjects had failed to uncover any deficit because visual information was presented to both hemispheres, and therefore the investigators had not been able to observe the problems associated with lack of communication between the two hemispheres.

The study of "natural lesions" in patients encounters other challenges in addition to many of the ones discussed in the previous section for animal work. Many human studies may be unique and hard to reproduce, depending on the exact nature of the lesion. There are plenty of single case studies. These studies are fascinating and highly informative. Yet, without reproducibility, it is not always easy to follow up or investigate the deficits in further detail, as can be done in studies in animals. Additionally, natural lesions do not necessarily respect any boundaries established by anatomical, cytoarchitectonic, or neurophysiological criteria. Therefore, many neurological lesions encompass large parts of cortex and multiple regions that are functionally distinct. The accidental nature of these lesions can make it challenging to interpret the findings due to the combination of multiple direct, indirect, and non-specific lesion effects. Another difficulty in human lesion studies is that it is not always easy to localize the lesion or brain abnormality. Magnetic resonance imaging (MRI) and computed tomography (CT) can only detect certain types of relatively large-scale brain transformations, but more subtle effects are typically missed.

Despite the limitations in researching human lesions, an advantage of human neurological studies over animal studies is the accessibility of subjective behavioral reports. In some cases, specific visual deficits after lesioning or silencing experiments in animal models may be hard to detect due to the limited nature of the behavioral assessment paradigms. Behavioral evaluation is often more straightforward in humans. In fact, human subjects may even come to the doctor and directly report the deficits in full detail.

IV.4. Partial lesions in primary visual cortex lead to localized scotomas

*INSERT **Figure IV-3** ABOUT HERE*

***Figure IV-3. Local blind spots (scotomas) caused by lesions in primary visual cortex**. (Left). Flattened map of primary visual cortex, in the occipital lobe, around the calcarine fissure. The map highlights different locations with different colors for reference to the visual field mapping on the right. (Right) Visual field map showing the position from the center of fixation (center of the circle) at different eccentricities. Note the disproportionately large fraction of cortex devoted to the small foveal area around fixation (red). Reproduced from Glickstein 1988.*

The scientific study of visual cortex is arguably the only positive outcome of the nefarious wars at the beginning of the twentieth century. The discovery of primary visual cortex can be traced back to the careful examination of bullet trajectories through the human brain and their behavioral consequences during the Russo-Japanese War and World War I. In the late 19th century, Hermann Munk (1839 – 1912), reported that damage to the occipital lobe in one hemisphere in monkeys rendered the animals blind in the contralateral visual hemifield (contralateral means the opposite side). During the early wars of the twentieth century, a Japanese physician named Tatsuji Inouye (1881–1976) and two British physicians named Gordon Holmes (1876–1965) and George Riddoch (1888–1947) described clear and delimited visual field deficits contralateral to the lesion in the occipital cortex. New weapons introduced during these wars caused bullets to penetrate the skull at high speeds without completely shattering the skull. Certain bullet trajectories going through the occipital lobe caused the soldiers to lose consciousness momentarily but ultimately recover.

Methodical scrutiny showed that patients suffering from wounds in the occipital cortex were essentially blind within a delimited part of the visual field, resulting in a *visual scotoma*, a black patch at a specific location with respect to the fixation location. Because positions are described with respect to the fixation point, the location of the scotoma in the world changes when the subject moves his/her eyes. Local damage in primary visual cortex gave rise to blind regions in the visual field, and the effects were quite similar to the ones observed due to local lesions in parts of the retina. Shape, color, and, to a lesser extent, motion discrimination, were typically absent within the scotoma. Similar effects are often encountered through vascular damage, tumors, and trauma studies of the occipital cortex. By correlating the visual deficits with brain damage, it was possible to establish a map of the visual field in the posterior part of the occipital lobe, an area that is now known as *primary visual cortex* or V1 (***Figure IV-3***). Biologists like to come up with names for genes, cell types, and brain areas; it is not unusual to have multiple names refer to the same thing. Visual area V1 is sometimes referred to as primary visual cortex, striate cortex, calcarine cortex, area 17 (in cats), and also Brodmann area 17 (based on the cytoarchitectonic maps subdividing cortex into multiple areas by the German neurologist Korbinian Brodmann (1868–1918) at the beginning of the 20th century). A rose by any other name would smell just as sweet.

The discovery of primary visual cortex was inspiring in many ways. First, it documented how a concrete function could be represented in a specific location in cortex. Together with localization studies for language functions dating back to the seminal work of Paul Broca (1824–1880), these findings provided ammunition to the idea that cortex is not merely an amorphous distributed sheet of computational elements but rather, that it is possible to ascribe specific roles to groups of neurons in specific locations. Second, going well beyond the localization of language functions, lesions in visual cortex showed a rather detailed topographic map between the outside world and the brain. Third, these

lesion studies set the foundation for the detailed neural circuit analyses that would come a few decades later and continues to this day, to be discussed in **Chapters V-VI**.

The amount of real estate in cortex devoted to different parts of the visual field is not distributed uniformly. There is a disproportionately larger area of V1 devoted to processing the fovea (red region in ***Figure IV-3***); this enlargement of the foveal representation is known as the cortical magnification effect. The fovea constitutes less than 0.1% of the total visual field size, but its representation takes almost 10% of primary visual cortex. There is progressively less amount of cortex per visual degree as we move from the center of fixation to the periphery. Having a high-resolution representation is good, but it comes at a cost. The brain would have to be orders of magnitude larger, hence heavier and more expensive from an energetic viewpoint, to represent the entire visual field with the same resolution as the fovea. The cortical magnification of the fovea, combined with rapid eye movements (**Section II.4**) and working memory (the ability to temporarily store information), provides an elegant compromise to obtain high acuity with a manageably-sized brain.

The visual field is mapped onto cortex in a topographical fashion: nearby locations in cortex represent nearby locations in the visual field. As noted earlier, information from the right hemifield is mapped onto the left visual cortex and vice versa. The *calcarine sulcus* divides primary visual cortex. A sulcus is a furrow, which gives rise to the convoluted shape of the brain and allows folding the vast expanse of the cortex into a tight volume. The upper hemifield (yellow in ***Figure IV-3***) is mapped onto the lower bank of the calcarine sulcus, and vice versa. Because of this orderly topographical organization, when an investigator lowers an electrode to record the activity of neurons in primary visual cortex (**Chapter V**), the anatomical landmarks provide an approximate guideline to localize the neuron's receptive field (i.e., the part of the visual field that activates the neuron, ***Figure II-9***). The topographical arrangement, usually referred to as retinotopic mapping in this case, can lead to saving wire, and hence also space, to establish all the connections to and from primary visual cortex. Additionally, because of this topography, coarse measurements that average the activity of multiple nearby neurons may still reveal interesting properties of the circuit, in contrast to a situation where all the neurons are arranged in a completely random fashion. Such a topographical organization is also a property of most, if not all, of the other visual cortical areas.

There was a considerable degree of excitement in the vision community a few years ago with the description of a phenomenon called *blindsight*. As the name suggests, it was observed that some subjects with profound lesions to occipital cortex were still capable of certain visual behaviors within the scotoma. Several possibilities were proposed to account for these observations, including anatomical routes that bypass V1 (for example those connecting the LGN to other visual cortical areas), and the presence of small intact islands in V1 that

may not be seen at the coarse scale of magnetic resonance images used to characterize the lesions. Although there is no doubt about the basic phenomenology of residual visual capabilities in patients with damage to V1, the range of visual behaviors in these subjects is limited. Subjects could detect motion (this was also observed in the initial study of soldiers with occipital cortex wounds by Riddoch in 1917), discriminate day from night, approximately localize a light source and describe its color, and other coarse visually-elicited behavior. However, in all cases, their capacity for fine visual discrimination was lost.

The profound deficits after V1 lesions in both animals and humans, combined with the challenges in examining visual behavior in animals, led several prominent investigators in the 1950s to argue that V1 is not only necessary but also sufficient for visual perception. In an interesting historical overview, Charles Gross cites several striking demonstrations of this narrow-minded scientific perception which turned out to be completely wrong: "In human subjects there is no evidence that any area of the cortex other than the visual area 17 [this is area V1] is important in the primary capacity to see patterns. . . . Whenever the question has been tested in animals the story has been the same."; "…visual habits are dependent upon the striate cortex [another name for area V1] and upon no other part of the cerebral cortex."; "… image formation and recognition is all in area 17 and is entirely intrinsic. … the connections of area 17 are minimal".

IV.5. What and Where pathways

The assertion that vision stops in area V1 was proven to be completely wrong. Multiple studies have shown that severe visual deficits can be ascribed to lesions in cortical areas outside of V1. One of the earliest demonstrations that V1 could not be the entire story was the study of the so-called Kluver-Bucy syndrome. After bilateral removal of the temporal lobe in macaque monkeys, the original reports described a variety of behavioral effects, including loss of visual discrimination, but also other symptoms such as increased tameness, hypersexuality, and altered eating habits. The wide variety of symptoms is now thought to be a consequence of massive and poorly circumscribed lesions. Subsequent and more refined lesion studies confirmed that lesions of the inferior temporal cortex lead to deficits in the ability to discriminate colors and shapes, without all the other accompanying non-visual manifestations.

Studies outside of V1 led to a fundamental distinction between lesions to *ventral cortex* and lesions to the *dorsal* cortex. The ventral cortex leads from V1 into area V4 and the inferior parts of the temporal cortex (mostly along the rightmost part of the diagram in ***Figure I-5***). The *dorsal cortex* leads from V1 into areas MT, MST, and parietal cortex structures (mostly along the middle and left part of the diagram in ***Figure I-5***). Ventral visual cortex lesions lead to deficits in shape recognition, and therefore this pathway is often referred to as the "What" pathway. Dorsal visual cortex lesions lead to deficits in object localization, and

therefore this pathway is often referred to as the "Where" pathway. As emphasized by the dense connectivity in ***Figure I-5***, these two pathways are not really independent, and there are multiple interconnections between the two.

IV.6. The "where" pathway: Dorsal stream lesions

The types of deficits associated with lesions along the dorsal visual stream are quite distinct from those associated with lesions along the ventral visual stream. The dorsal pathway is mainly involved in spatial localization of objects within their environment and detecting object movement. Lesions along the dorsal stream can lead to akinetopsia, neglect, hemineglect, optic ataxia, and simultanagnosia.

Akinetopsia refers to the specific inability to discriminate visual motion. This condition has been likened to the perceptions evoked by stroboscopic lights in a discotheque. The subject with akinetopsia can see isolated snapshots but not the movement trajectory. This condition has also been reproduced in monkeys upon lesioning of the MT area in the dorsal path.

Visual *hemineglect* is described as an attentional disorder and is associated with lesions in the parieto-occipital junction. Hemineglect is defined as the inability to attend to a visual hemifield contralateral to the side of the lesions. For example, a subject may eat from only the right half of the plate or may copy only one half of a drawing. The condition is rather curious: the subjects are *not* blind in one hemifield, as demonstrated by the fact that subjects can be made to attend and identify objects in the affected hemifield. Furthermore, and particularly intriguingly, some hemineglect patients also fail in tasks that involve retrieving information from visual memories in a location-specific manner. In a famous experiment, an Italian subject with left-sided hemineglect was asked to imagine standing in the Piazza del Duomo in Milan, facing the famous cathedral, and report what they could recall from this scene. Subjects typically omitted to mention places or streets on the left side from that vantage viewpoint.

Simultanagnosia is the inability to see more than one or two objects in a scene. Sometimes subjects are only able to detect small parts of objects. Subjects with simultanagnosia are not able to interpret a visual scene. The impairment is so debilitating that these subjects are often described as being functionally blind despite showing perfect acuity for the object that they are attending to at any given time.

All of these conditions are extremely infrequent in the population. We can argue that in all of these conditions, object shape recognition remains intact. Because of the motion discrimination deficits, and the spatial aspects of neglect, the dorsal visual cortex is described as the *Where* pathway. An alternative, but not necessarily mutually exclusive description, refers to dorsal visual cortex as the *Action* pathway. Melvyn Goodale and David Milner described an unusual

patient with a lesion primarily restricted to the temporal lobe. This subject had severe impairment in object shape recognition, as we will describe in the next section. However, despite her inability to recognize objects, the subject showed a rather remarkable ability to interact with many objects. For example, she showed an appropriate reach response towards objects that she could not describe. She also showed correct behavioral performance in visuomotor tasks. Goodale and Milner proposed that the dorsal pathway is particularly engaged in "vision for action," the immediate use of visual information to carry out specific visually guided behaviors. In contrast with this action mode, they proposed that awareness about an object requires activity in the ventral stream and the temporal lobe in particular.

IV.7. Inferior temporal cortex is critical for visual object recognition in monkeys

The confusions around the Kluver-Bucy syndrome illustrate the challenges in interpreting the consequences of large cortical lesions. Making more precise lesions restricted to inferior temporal cortex (ITC) has shown that bilateral ITC removal leads to impairment in learning visual discriminations as well as deficits in retaining information about visual discriminations that were learned before the lesions. In typical experiments, monkeys have to learn to discriminate between different visual shapes to obtain a reward. Animals with lesions in ITC fail in this task, but they can still perform other visual tasks such as learning which one of two visual locations is associated with reward.

The severity of the deficit is typically correlated with task difficulty. Monkeys can still perform "easy" visual discrimination tasks after bilateral ITC lesions. Deficits apply to objects, visual patterns, object size, color, and other properties. Deficits in recognizing forms defined by motion or luminance have also been described after ITC lesions. The behavioral deficits are restricted to the visual domain and do not affect discrimination based on tactile, olfactory, or auditory inputs. None of the "psychic blindness" or other social effects described originally by Kluver and Bucy were apparent after bilateral ITC lesions, further emphasizing the importance of spatially restricted lesions to adequately interpret the behavioral deficits. These visual shape recognition deficits are long-lasting.

Scrutinizing the anatomical pathways described in **Figure I-5**, we observe that there are many ways for information to travel from one point to another in visual cortex. Information could be flexibly routed throughout the visual circuitry, depending on the nature of the task at hand. In the absence of ITC, certain "easy" tasks could be solved by routing information from early visual cortical areas onto decision and motor centers. Other more "complex" tasks may necessitate the type of computations that take place in higher areas like the ITC.

In the same way that the Kluver-Bucy syndrome could be fractionated by more circumscribed lesions, it is quite likely that future, even more specific, lesions within ITC will further fractionate the object recognition deficits prevalent after bilateral ITC ablation. Indeed, hints of this type of specificity are apparent in recent elegant work combining pharmacology, optogenetic manipulation, neural recordings, and behavior in monkeys. Investigators focused on an area of ITC cortex with an abundance of neurons that respond preferentially to faces compared to other objects (a theme that we will return to when we examine the neurophysiological properties of ITC neurons in **Chapter VI**). To the extent that the activity of those neurons is instrumental in tasks that depend on understanding face shapes, the authors hypothesized that inhibiting local regions would disrupt behavioral performance in suitable recognition tasks. To evaluate this hypothesis, they trained monkeys in a gender discrimination task based on face images. Once the animals were trained, the authors inactivated small local regions of ITC. This inactivation was performed using either optogenetic manipulation or pharmacological intervention. Suppressing local neural activity led to an impairment in gender discrimination performance in the monkeys. These behavioral effects were reversible: performance returned to normal levels after the optogenetic or pharmacological silencing was turned off. The effects were also specific: inactivation of other brain regions did not lead to such behavioral impairments. In sum, lesion studies point to an essential function of ITC in the ability to discriminate different shapes visually. Such studies played an important role in guiding the neurophysiological investigation of the properties of ITC neurons during visual recognition (**Chapter VI**).

IV.8. Lesions leading to shape recognition deficits in humans

*INSERT **Figure IV-4** ABOUT HERE*

***Figure IV-4. A patient with visual form agnosia who struggles to draw shapes**. The patient was asked to draw **A**. His name; **B**. Letters W, V, L, X, and A; **C**. Number 1 through 11; **D**. a circle, square, and triangle; **E**. A man. (Reproduced from Benson 1969)*

Due to experimental challenges, much less is understood about the consequences of lesions to human ventral visual cortex. Along the ventral visual stream, lesions around area V4 lead to a*chromatopsia*, a specific inability to recognize colors. Note that this condition is distinct and dissociable from the type of retinal color blindness discussed in **Chapter II**, which is associated with a lack of one or more types of cones.

Lesions in higher areas of the temporal lobe can lead to a variety of intriguing forms of *agnosias* (Agnosia means “lack of knowledge” in Greek). ***Figure IV-4-6*** illustrate the type of behavioral deficits encountered in one type of visual agnosia in three different tasks. These figures illustrate the behavior of a 25-year-old patient who was examined seven months after accidental carbon monoxide poisoning. The patient was able to navigate the hospital where he was admitted, he could follow moving objects, and he could name colors. There were

no abnormalities in the retinae. His visual fields, that is, his ability to detect flashes of light in different locations with respect to fixation, were mostly normal.

Although those elementary visual functions were intact, the patient was unable to name objects placed in front of him. He could still name objects by using tactile, olfactory, or auditory cues, suggesting that the deficit was not associated with an inability to produce speech or to retrieve semantic information about objects. He was unable to make drawings of specific shapes, including writing his name or drawing a man (***Figure IV-4***). The inability to draw specific shapes upon request could potentially be ascribed to a specific deficit in retrieving visual memories. However, the patient was also unable to copy shapes using templates presented in front of him (***Figure IV-5***). The patient could clearly understand language and could also execute motor commands. One may still argue that the tasks in ***Figure IV-4*** and ***Figure IV-5*** rely on the ability to draw, and people may have different abilities to draw. However, the same patient was able to make better drawings, and certainly to write his name, before the accident. Furthermore, the patient also struggled in a visual shape matching task that did not require any drawing (***Figure IV-6***).

INSERT ***Figure IV-5*** *ABOUT HERE*

Figure IV-5. The same patient cannot copy shapes*. The patient was asked to copy the letters and numbers in column 1 and the shapes in column 3 (Reproduced from Benson 1969).*

As noted earlier, ***Figure IV-4-6*** describe a single case study. Not all subjects with agnosias have the same deficits. For example, some patients can do an excellent job in the copying task (***Figure IV-5***), but not in the drawing from memory task (***Figure IV-4***). It is not clear whether this type of deficit should be described as a visual impairment, or rather a language deficiency, a visual imagery challenge, or a difficulty in retrieving shapes from memory. The type of generalized deficit with shapes combined with normal visual field and adequate language and memory function in other sensory modalities, as illustrated by the patient in ***Figure IV-4-6*** is rare but seems to suggest a *bona fide* visual impairment.

INSERT ***Figure IV-6*** *ABOUT HERE*

Figure IV-6. The same patient fails to perform a visual shape-matching task*. The patient was asked to indicate which of the objects matched the one on top in each column (Reproduced from Benson 1969).*

These types of studies often involve single subjects or a handful of subjects, and the lesions are necessarily not well circumscribed. Shape recognition agnosias have been subdivided into mmultiple groups depending on whether they are thought to be mostly visual, whether the deficits also involve language, and whether the deficits affect object manipulation or recognition through other sensory modalities. One variant is called *associate visual agnosia*. This label is assigned to cases where copying a drawing and matching complex

shapes remain intact, but drawing from memory and object identification are significantly impaired. As mentioned above, in many of these studies, it is not entirely clear that the deficits are strictly associated with the visual recognition machinery. Patients may show deficits in naming the stimuli, describing them, using them, drawing them from memory – all tasks that may depend on or relate to language abilities – but not necessarily matching two similar objects based on visual appearance or copying them. Another variant is called *aperceptive visual agnosia*. These subjects cannot name, copy, or match simple shapes. Because they cannot copy or match shapes, these cases may be closer to visual recognition challenges, such as the specific patient considered in ***Figure IV-4-6***.

Importantly, in many of these visual agnosia cases, basic visual function remains intact. Visual acuity, the ability to recognize colors, the ability to detect motion, and other visual functions do not seem to be affected. This double dissociation between "basic" visual functions and "higher level" visual abilities is consistent with the idea of a hierarchy of computations that progressively extracts more complex features from an image, from early image processing in the retina, LGN, and primary visual cortex, all the way to structured shape information in the inferior temporal cortex. Indeed, the visual agnosias are typically associated with bilateral damage to visual areas beyond area V1, typically including the inferior temporal cortex. As noted in the previous section, it is likely that many of these basic visual functions can be implemented via connections in ***Figure I-5*** that bypass ITC.

Would subjects with visual agnosia struggle with the drawing and shape matching tasks for *any* type of object? How specific are the agnosias? Intriguingly, several studies have reported cases of category-specific agnosias. For example, some studies report a more significant deficit in recognizing "living things." Other studies describe an inability to recognize animals, tools, words, or landmarks. One study reported a patient with an inability to name fruits or vegetables presented through line drawings or photographs. The literature on human lesion studies relating to visual symptoms points to remarkable and sometimes highly specific deficits in visual shape recognition.

One specific form of agnosia has received particular attention in the literature. *Prosopagnosia* (Proso (Greek): face) refers to the inability to visually recognize faces with intact ability to identify other objects and shapes. Face agnosia is also very rare and typically occurs after brain damage caused by strokes in the right posterior cerebral artery. Some studies have also described a congenital form of prosopagnosia. The fusiform and lingual gyri are typically affected. Oliver Sacks emphasized the extreme nature of prosopagnosia in his narrative about "*The man who mistook his wife for a hat.*" Prosopagnosic subjects are often able to recognize people based on their voices, clothes, gait, and other characteristics but not from photographs of the face. The extent to which the effects should be described as face-specific has been debated extensively. Some authors argue that the impairment in face recognition can be

better understood as a general difficulty in identifying exemplars from a class with many similar stimuli and the degree of expertise with those stimuli.

IV.9. Invasive electrical stimulation of the human brain

*INSERT **Figure IV-7** ABOUT HERE*

Figure IV-7. Creating visual percepts by injecting currents into visual cortex. *Position of phosphenes (light flash sensation) in the visual field elicited by electrical stimulation in human occipital cortex. The center circle indicates the fovea, and the numbers identify the electrodes through which electrical stimulation pulses were delivered. The symbols coarsely denote the size and shape of the elicited phosphenes. Reproduced from Brindley and Lewin, 1968.*

Lesions are not the only way to study the causal function of a given brain area. We switch gears now to consider another way of interfering with brain function: injection of electrical currents. Wilder Penfield (1891–1976) was one of the key figures in the invasive study of the human brain through his work with epilepsy patients. As a neurosurgeon, he realized that he had direct access to the inner workings of the human brain through his neurosurgical approach to epilepsy. He worked extensively with patients suffering from pharmacologically resilient epilepsy. In these patients, seizures cannot be stopped by current methods of pharmacological intervention. In these cases, one of the best approaches to eliminate seizures is to remove the epileptogenic focus, that is, the part of the brain where seizures originate. In order to perform this type of resection, the neurosurgeon has to be able to localize the epileptogenic focus and also functionally map the area to ensure that there will not be any other adverse cognitive symptoms as a consequence of the procedure. Guided by these clinical needs, neurosurgeons invasively implant multiple electrodes in these patients; the patients stay in the hospital for about one week, with their electrodes in place in order to accumulate sufficient data. During this week, it is possible to interrogate human brain function with a much better signal-to-noise ratio, much better spatial resolution, and much better temporal resolution than any other method to study human brain activity from the outside.

Because the epileptogenic focus is resected in most of these patients, it is also possible to study the behavioral consequences of removing a part of the brain. One of Penfield's seminal studies described the role of the medial temporal lobe in memory consolidation in patients that underwent bilateral removal of the hippocampus and surrounding areas. Removal of the hippocampus on both hemispheres leads to severe problems in memory consolidation: the patient can see and visually interpret the scene normally, can hold a normal conversation, can reason, and perform a variety of cognitive tasks. In fact, after talking with such a patient for a few minutes, it would be hard to detect anything out of the ordinary. Even though the hippocampus appears at the pinnacle of the anatomical diagram of the visual system in ***Figure I-5***, all the evidence to date suggests that the hippocampus is not a visual area. The distinct characteristics of patients with bilateral excisions of the hippocampus are only manifested when

considering the memory system. If you were to talk to the same patient the next day, the patient would have no recollection of what had happened during your first meeting. Because of those studies, only unilateral resections are performed nowadays.

Penfield was also one of the pioneers in performing neurophysiological recordings from intracranial electrodes in the human brain. Furthermore, he also extensively studied the behavioral effects triggered by electrical stimulation through subdural electrodes while the subjects were awake and readily reported their percepts. Electrical stimulation is a standard procedure that is used routinely in hospitals throughout the world. Because there are no pain receptors in the brain, this is not a painful procedure, and subjects can be awake during brain surgery, which often turns out to be quite useful from a clinical standpoint. It is quite important in these cases to work with subjects who are awake to be able to map cognitive function before resection. In particular, neurologists and neurosurgeons are concerned about language functions, which often reside close to epileptogenic areas. The goal is to treat epileptic seizures without affecting any other cognitive computation. One of the most famous discoveries from Penfield based on these electrical stimulation studies is the *cortical homunculus*, a mapping of the human body in the motor and somatosensory areas around the precentral gyrus.

Upon stimulating a given location, he asked the subjects to report their sensations verbally. Penfield would identify the stimulation locations by numbers. For example, the first time he stimulated electrode "5," the patient did not reply. Upon a second stimulation pulse in the same location, the patient said, "Something." The fourth time, he reported hearing, "People's voices talking." Penfield switched to electrode "7". The first pulse in electrode "7" elicited the following response: "Like footsteps walking – on the radio." Upon the third stimulation pulse in electrode "7", the subject explained, "it was like being in a dance hall, like standing in the doorway – in a gymnasium – like at the Lenwood High school." Twenty minutes later, Penfield moved back to electrode "5," and the subject reported, "People's voices."

Some of the observations are transcribed here *verbatim* to illustrate the exciting opportunities in terms of the questions that we can ask by obtaining direct verbal reports from stimulating human cortex. At the same time, the example illustrates how challenging it is to interpret the output of these fascinating but anecdotal reports. What exactly is being stimulated in these studies? How many neurons are activated? What type of neurons are activated? How reproducible are the effects over multiple repetitions? How does the answer to these questions, and the ensuring behavioral reports, depend on the parameters of stimulation like the pulse duration and intensity? How do the conclusions depend on the metrics used to assess the behavioral output? What does the subject feel during electrical stimulation? To what extent is the subjective report influenced by the environment (doctors, nurses, hospital)? How

can we map these fascinating reports obtained via electrical stimulation to our understanding of the functions of cortex? There is a rich experience lost in translation.

In some cases, electrodes are placed in parts of the visual cortex. Particularly when electrodes are placed in early occipital cortex, several investigators have demonstrated that it is possible to elicit perceptual light flashes denominated "phosphenes." An example of such an experiment is illustrated in ***Figure IV-7***. Upon injecting currents, the subject was asked to report the shape and location of what they perceived. In most cases, the subject reported seeing approximately circular flashes of light, in a few cases like electrode 9, subjects reported seeing elongated lines. We briefly alluded to neurons in primary visual cortex (V1) showing tuning for lines of different orientations in **Chapter I**, and we will discuss neuronal tuning preferences in more detail in **Chapter V**. Based on the idea that V1 neurons are excited by oriented bars, one may expect to see more lines in ***Figure IV-7***. However, these coarse stimulation experiments probably activate an enormous number of neurons, probably encompassing many, if not all, orientations. Therefore, it is not too surprising that the main report does not show much feature specificity.

Interestingly, the perceptual experience triggered by stimulating early visual cortex is consistent with our understanding of the topographic organization derived from lesion studies described above (***Figure IV-3***). This organization is also consistent with the neurophysiological recordings that we will discuss in **Chapter V**. First, the location of phosphene experiences in the visual field depends on the exact area of stimulation. Those phosphenes are localized, consistent with the idea that multiple neurons with overlapping and constrained receptive field sizes are being activated. Second, injecting currents through nearby electrodes (e.g., electrodes 27, 31, 34, 35 in ***Figure IV-7***) triggers phosphene sensations in nearby locations in the visual field, as we would expect based on the topographical organization of visual cortex. Third, the approximate size of the experienced phosphene increases as we move away from the fixation, consistent with the increased receptive field sizes as a function of eccentricity.

Following up on the seminal studies of Penfield, several other investigators used electrical stimulation in epilepsy patients to map function in human cortex. For example, investigators have described multiple subjective experiences elicited after stimulation of the temporal lobe, including visual illusions, both elementary visual hallucinations (phosphenes), and complex visual hallucinations. In addition to visual illusions, electrical stimulation in the temporal lobe elicits a large number of other experiences, including fear, thirst, familiarity, the feeling of déjà vu, and memory reminiscences.

An elegant study by Murphey and colleagues further examined the relationship between electrical stimulation and neurophysiological recordings. They examined an area that responded to colors, more specifically, to the blue

color, according to neural recordings. They subsequently used a psychophysical task to ask whether subjects could determine the effects of electrical stimulation. Subjects reported perceiving a blue hue upon electrical stimulation, consistent with what the authors predicted based on their neurophysiological findings.

Phosphenes, visual hallucinations, and perception of color are examples of a novel perceptual sensation elicited by the injection of current in the absence of concomitant visual stimulation. Many other studies have focused on evaluating the effects of stimulation over a concomitant visual stimulus. In such cases, results show that electrical stimulation typically interferes with the current percept. For example, several studies have shown that applying electrical stimulation through electrodes near the fusiform gyrus distorts or impairs the ability to perceive faces.

IV.10. Electrical stimulation in primate visual cortex

While the possibility of electrically stimulating human cortex is quite exciting, a lot of the observations have been fascinating, yet mostly anecdotal, due to the difficulties inherent to a low number of trials and large electrodes with coarse mapping to neuronal responses. Many investigators have used electrical stimulation through microelectrodes in the macaque monkey visual cortex. The type of microelectrodes used in animal studies is smaller (about 50 microns in diameter) than the ones used in humans (about 2 millimeters in diameter; only a handful of cases have used microelectrodes for stimulation in the human brain). Thus, the number of neurons activated via electrical stimulation in animal studies, though still very large, is smaller than the number of neurons excited in human studies.

*INSERT **Figure IV-8** ABOUT HERE*

***Figure IV-8. Schematic representation of an electrical stimulation experiment in area MT of the macaque monkey. A**. Schematic responses of a neuron that responds selectively to leftward motion. **B**. Random dot stimuli with no coherence (left), high leftward motion coherence (right), and medium leftward motion coherence (center). **C**. Reported perception in the absence of electrical stimulation. **D**. Hypothesized perceptual reports when stimulating neurons around the one shown in part A (based on the work of Salzman et al. (1990)).*

One of the seminal studies in monkeys involved electrical stimulation of the MT area, which we introduced in **Section IV-2** as an area critical for motion discrimination based on physical lesions in monkeys, and in **Section IV-6** as the likely area responsible for impaired motion perception in akinetopsia. Area MT receives direct input from area V1 (and also inputs from other areas like V2), coming from the magnocellular layers in the LGN. Neurons in area MT are selective for motion direction within the receptive field; for example, a neuron may respond strongly to a bar moving to the left and not to a bar moving to the right (***Figure IV-8A***).

A typical stimulus used to drive MT neurons is a display consisting of many dots moving in random directions (***Figure IV-8B***). A given percentage of the dots is set to move coherently in one direction. Depending on the percentage of coherent motion, the stimulus can elicit a strong motion percept. A typical sigmoid psychometric curve can be plotted (both for humans as well as monkeys), showing the proportion of trials in which the subject reports that the dots are moving in one direction as a function of the degree of coherence of the dots in the display. If 100% of the dots move coherently in one direction, subjects report movement in that direction in all the trials. If 0% of the dots move coherently (all dots are moving randomly), then subjects report random movement in one direction or the other (***Figure IV-8C***).

William Newsome's team at Stanford trained monkeys to report their perceived direction of motion while recording the activity of neurons in area MT. Recording from in area MT, the investigators started the experiment by mapping a neuron's preferred direction of motion. In a typical experiment, a fixation spot comes up, monkeys are required to fixate, the visual stimulus is displayed for one second, the stimulus disappears, and the monkey needs to indicate the direction in which the dots were moving in a two-alternative forced-choice paradigm (e.g., by making a saccade to one of two possible targets). The direction of motion in each experiment is aligned to the neuron's preferred direction so that the dots move either in the preferred direction or in the anti-preferred direction.

*INSERT **Figure IV-9** ABOUT HERE*

Figure IV-9. *Results of an electrical stimulation experiment in area MT of the macaque monkey. The plots show the behavioral psychometric function in discriminating the neuron's preferred motion direction in the presence (filled circles) or absence (empty circles) of electrical stimulation (see text for details). Reproduced from Salzmann et al. (1990).*

Based on the neurophysiological recordings, the investigators asked whether electrical stimulation through the same microwire would bias the monkey's visually evoked behavior in the motion discrimination task and whether this bias would be consistent with the neurophysiological preferences. To answer this question, they applied very brief electrical pulses (10 μA biphasic square pulses with 200 Hz frequency and 0.2 msec duration). Electrical stimulation was applied in the center of regions where there was a cluster of neurons with similar motion preferences within ~150 μm. As in other parts of neocortex, there is a topographical organization of neuronal preferences in area MT, that is, nearby neurons in MT typically have similar motion direction preferences. This topography is presumably important in terms of understanding the effects of electrical stimulation because activating many local neurons with similar tuning properties may lead to stronger behavioral effects than activating neurons that are spatially organized in a completely random fashion with respect to their tuning properties. Monkeys were rewarded on correct responses. The results of such experiments are illustrated in ***Figure IV-9***. In the absence of microstimulation (empty circles), monkeys showed the typical approximately

sigmoid psychometric curve. Monkeys reported the preferred direction of motion in >80% of the trials when the dots had 30% correlation in the preferred direction, and they reported the anti-preferred direction of motion in >80% of the trials when the dots had 30% correlation in the anti-preferred direction. In the 0% correlation condition, monkeys reported one or the other direction with close to 50% performance. Remarkably, upon applying electrical stimulation (filled circles), there was a shift of the psychometric curve. Monkeys reported movement in the preferred direction more often (~15% more often) than in the absence of electrical stimulation. This causal increase due to electrical stimulation is a significant finding because it provided compelling evidence that the neurophysiological recordings revealed a signal that could translate into behavioral decisions upon electrical stimulation of the relevant neuronal circuits.

In a similar experiment, Arash Afraz and colleagues stimulated macaque inferior temporal cortex during a visual recognition task. The lesion studies indicate that the ITC area is important for visual shape recognition (**Section IV.7**). The experiment followed the structure of the Newsome study in ***Figure IV-8-9***. Because neurons in ITC are more interested in complex visual shapes rather than motion direction, the investigators compared responses to faces against responses to other shapes. The choice of faces as one of the two stimuli may have been an important methodological point. First, it may be easier to train monkeys to recognize 2D renderings of faces compared to other shapes. Second, there may be a larger cluster of neurons responding to similar faces compared to other shapes. The investigators presented faces and other non-face images embedded in noise. The noise level changed from 100% (pure noise stimulus) to 20%; noise in this experiment plays a similar role to coherence in the Newsome experiments.

As we will discuss in **Chapter VI**, ITC neurons showed visually selective responses; the investigators focused on sites that revealed consistent enhanced responses to faces within an area of approximately $\pm$ 150 μm. The investigators applied electrical stimulation in those regions and evaluated the extent to which the monkeys reported seeing faces or not for stimuli with different levels of noise. On average, the investigators were able to elicit a ~10% change in the monkey's behavior, increasing the number of times that the monkeys reported seeing faces (even in cases where information about faces was minimal due to the noise). Furthermore, the behavioral effects elicited by electrical stimulation were correlated with the degree of selectivity of the neurons: stimulation of more selective sites led to stronger behavioral biases.

In sum, across different areas within visual cortex, injecting currents into many neurons that show selectivity for specific stimulus features can bias a monkey's responses towards reporting seeing those specific features. Even in cases where the stimulus consists of random noise, it is possible to bias behavior in a way that can be predicted by the neurophysiological responses. These experiments provide a strong causal link between specific and selective neural

activity and visual perception. Additionally, these experiments constitute an intriguing form of injecting specific visual thoughts into the brain.

IV.11. Summary

- Inactivating areas of visual cortex leads to specific visual deficits ranging from localized *scotomas* (primary visual cortex) all the way to impairment in recognition of complex shapes (inferior temporal cortex).

- Without primary visual cortex, subjects are essentially blind. Very limited and basic visual capabilities remain in the absence of primary visual cortex.

- Lesion studies have delineated two main processing streams: (1) a *dorsal/where/action path* that is particularly relevant to detecting motion, interpreting stimulus locations, and spatially acting on visual stimuli, and (2) a *ventral/what path* that is more concerned with discriminating colors and shapes.

- Although brain lesions in humans are difficult to fully interpret due to their rarity and accidental nature, they have revealed a plethora of fascinating observations mapping visual deficits to localized circuits in the brain.

- Several cases have been reported of *agnosias* where subjects have specific visual discrimination challenges while maintaining otherwise normal vision.

- Electrical stimulation in early human visual cortex leads to the perception of *phosphenes*. The location and size of those phosphenes are consistent with our understanding of the topographical organization of early visual cortex.

- Stimulating other parts of human visual cortex during concomitant presentation of a visual stimulus can lead to specific perceptual disruption.

- Microstimulation experiments in monkeys have shown that it is possible to bias the animal's behavior in a way that is consistent with predictions based on the neurophysiological responses of neurons in the stimulated area.

IV.12. Further reading

See http://bit.ly/3abKBpP for more references.

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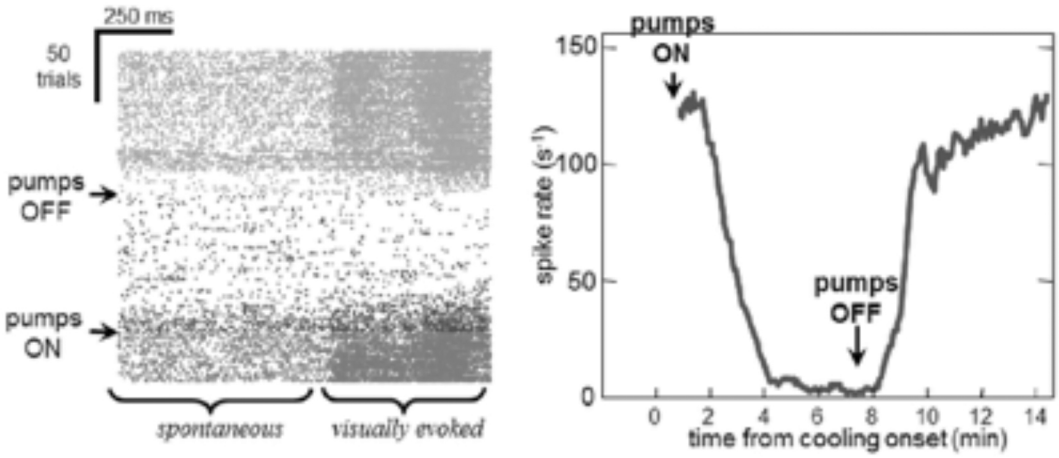
Figure IV-1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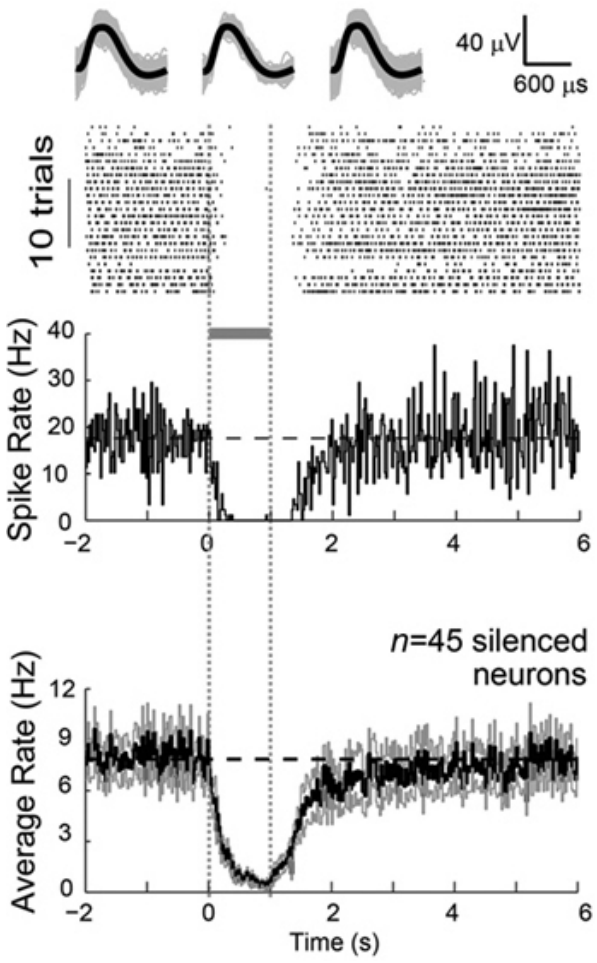
time from cooling onset (min)

Figure IV-2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n=45 silenced neurons
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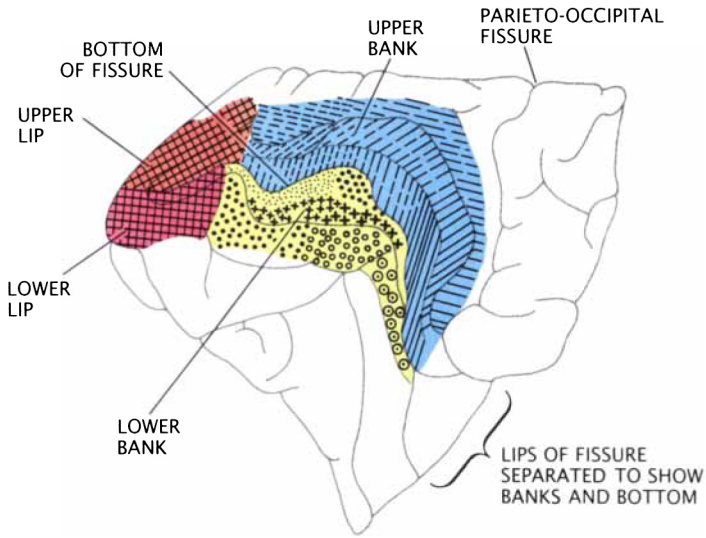
Time (s)

Figure IV-3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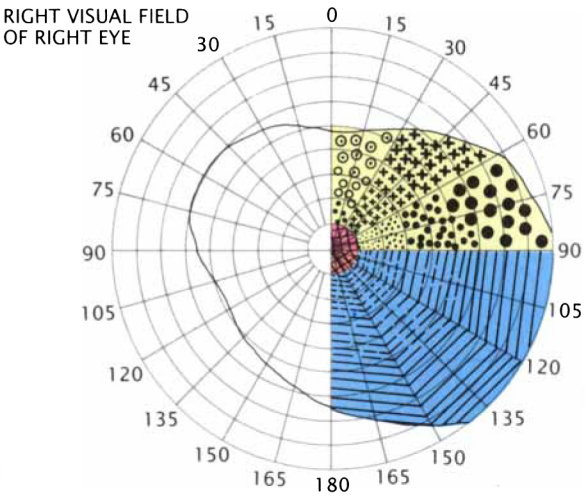
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Figure IV-4

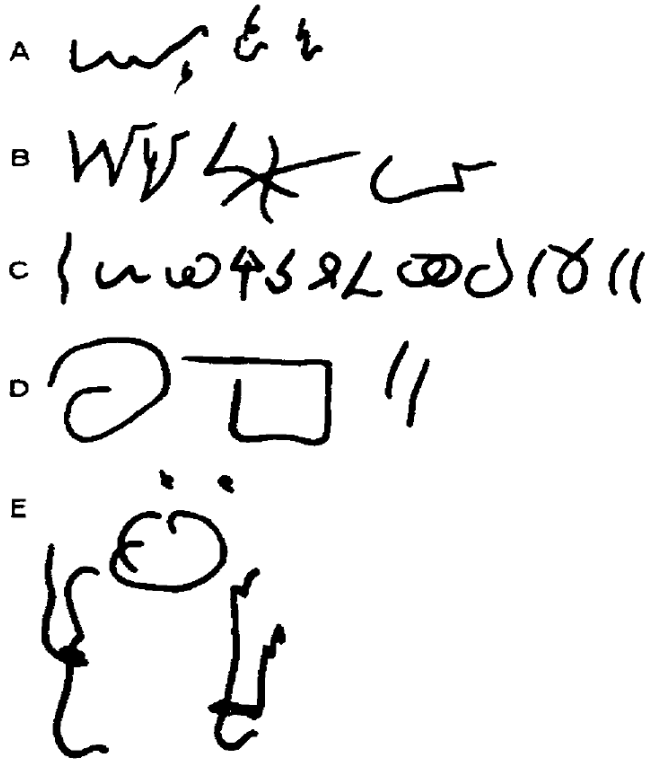

Figure IV-5

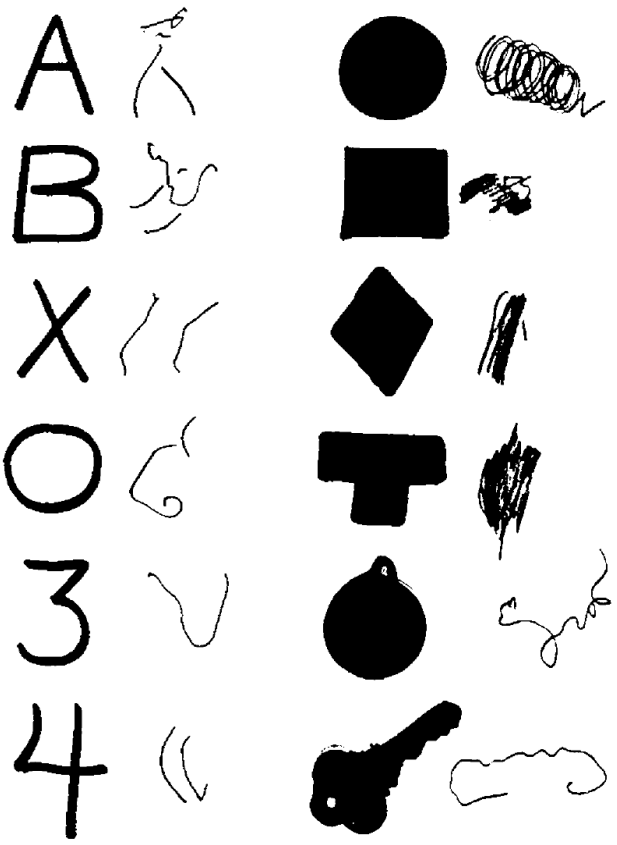

Figure IV-6

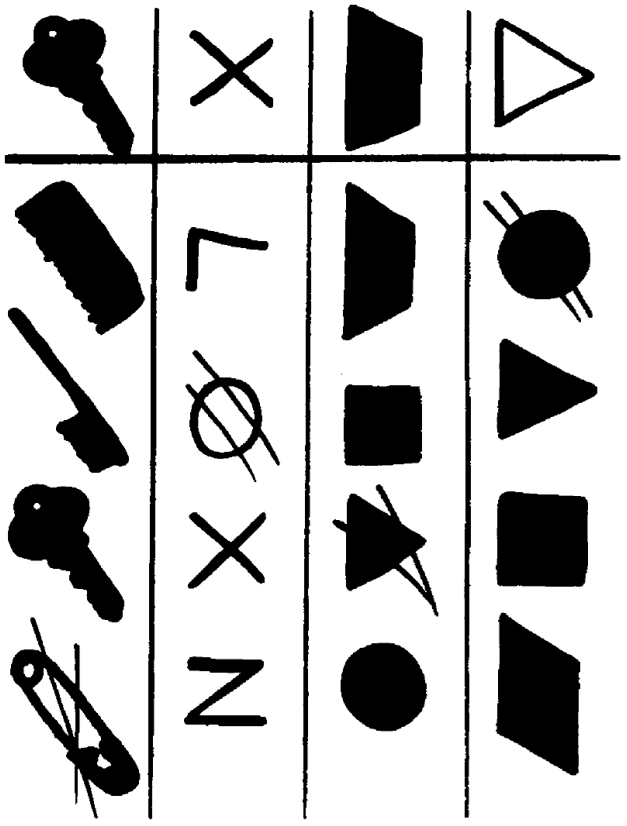

Figure IV-7

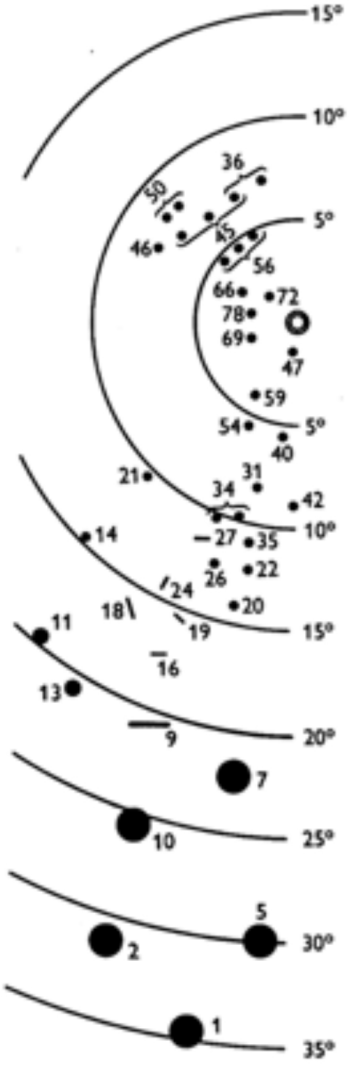
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Figure IV-8

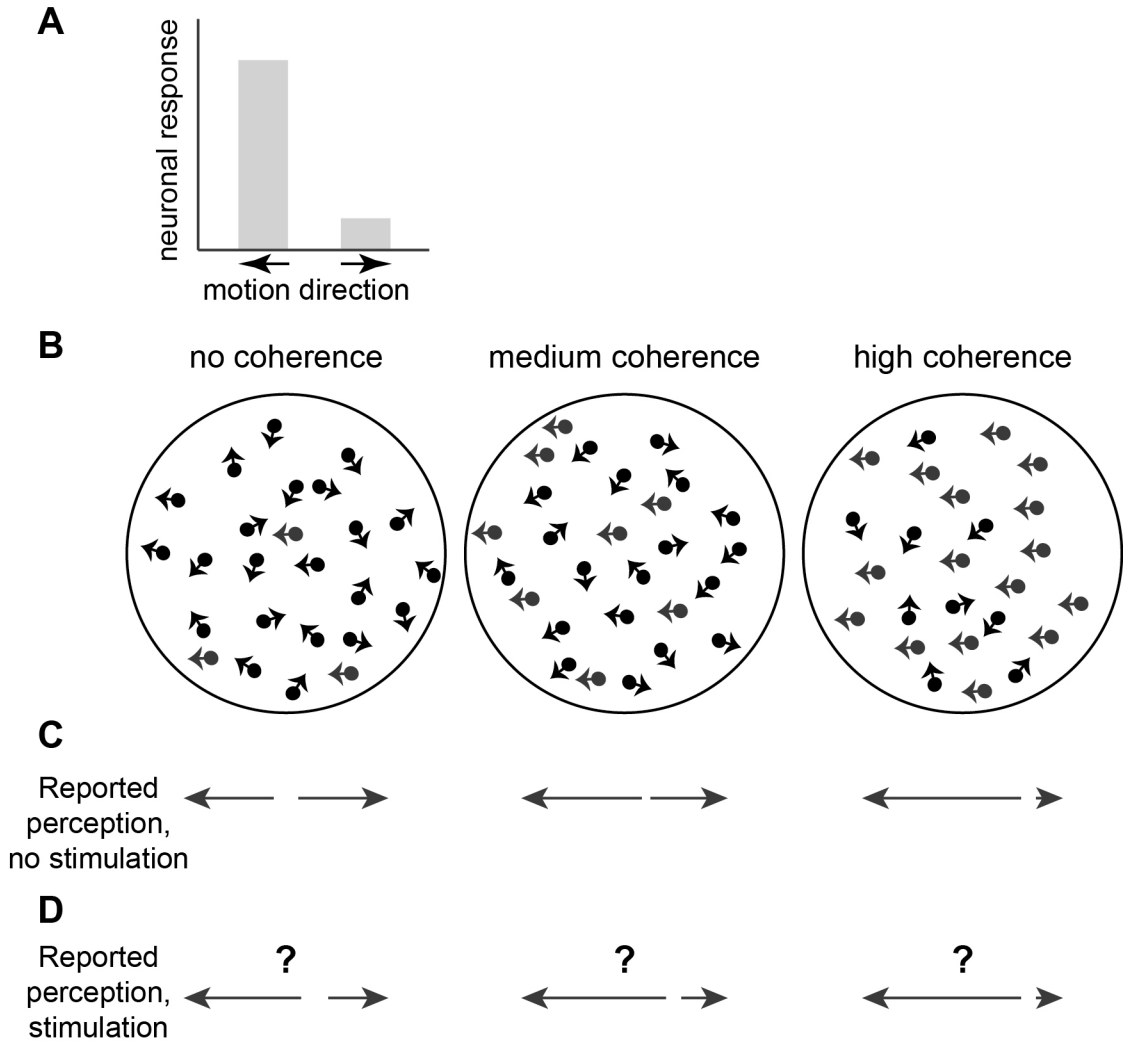
A
neuronal response
motion direction
B
no coherence
medium coherence
high coherence
C
Reported perception, no stimulation
D
Reported perception, stimulation
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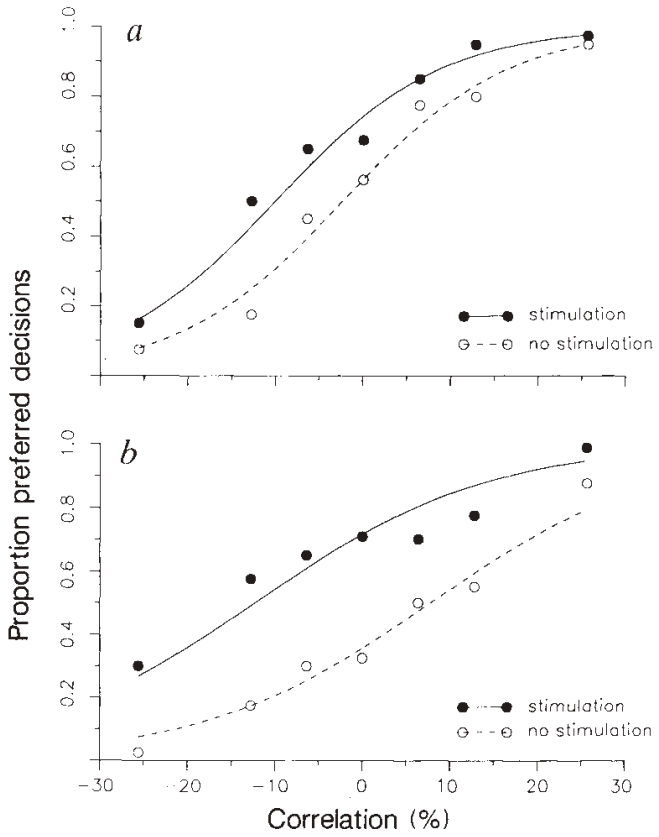
Figure IV-9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b
stimulation
no stimulation
stimulation
no stimulation
Proportion preferred decisions
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0.4
0.6
0.8
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−30
−20
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0
10
20
30
Correlation (%)