3 The Hallucinating Brain: Neurobiological Insights into the Nature of Hallucinations

Dominic H. ffytche

Abbreviations

CBS Charles Bonnet Syndrome
AMD Age-related macular degeneration

Abstract

Charles Bonnet's eighteenth-century philosophy of hallucinations was ahead of its time. Bonnet argued that hallucinations were caused by activity within specialized functional units serving both normal perception and hallucinations, a view largely supported by recent imaging evidence. Here I describe Bonnet's theory and the brain activity underlying visual hallucinations that occur in a condition named after him—the Charles Bonnet syndrome. The brain activity challenges our current view of hallucinations. It reveals similarities between the neural substrate of hallucinations, illusions, and afterimages, but differences from that of imagery, a finding seemingly inconsistent with current philosophical and clinical classificatory schemes. The activity also casts doubt on the assumption that hallucinations are reactivated memories. Finally, the wider clinical perspective questions our view of hallucinations as a single category of experience. Future theories of hallucinations need to be sufficiently broad to encompass a range of phenomena traditionally held as distinct, while sufficiently narrow to refer to specific neurobiological mechanisms. A single neurophilosophical account of hallucinations will not suffice; we need a family of theories.

1 Introduction

Hallucination on Crete marked the 250th anniversary of an important event in the history of scientific and philosophical inquiry into hallucinations. In the autumn of 1758, Charles Lullin, a retired Genevan magistrate, experienced the last of the visual hallucinations that had fascinated him since February of that year. His grandson Charles Bonnet, recently turned philosopher from biologist, recognized the significance of the experiences and encouraged Lullin to document them in a diary. Bonnet understood that hallucinations provide important evidence as to the nature of perception and how it relates to brain activity, and he derived a theoretical account of hallucinations that differs little from our current view. Here I describe Bonnet's theory and the clinical disorder referred to today as the Charles Bonnet syndrome. I then compare the brain activity underlying this type of hallucination to activity associated with other categories of visual perceptual experience in an attempt to reveal something of what hallucinations are and what they are not.

2 Charles Bonnet

Although Charles Bonnet (1720–1793) received a doctorate in law, his main early interest was the natural sciences. He became interested in entomology at age sixteen, and by twenty he had become the youngest corresponding member of the French Academy of Sciences for his description of parthenogenesis in aphids. A decade later, at the height of his natural science career, he was forced to abandon his studies because of an eye condition that made it increasingly difficult for him to use a microscope. He turned to philosophy, focusing first on psychology and the relationship between mind, brain, and soul. Later works placed greater emphasis on religion and a classificatory theory of past and future life on earth and heaven.

2.1 Eighteenth-Century Sensationism

Charles Bonnet's philosophical works fall in the tradition of sensationism, an extension of Locke's seventeenth-century empiricism championed in eighteenth-century French philosophical circles by Étienne Bonnot, Abbé de Condillac (1715–1780). For Locke (1690), *sensation* was the source of knowledge of external objects, while *reflection* was the source of knowledge of internal mental operations, a hierarchical taxonomy of ideas deriving from these two primary sources. Sensationists argued that Locke's reflection could be derived from sensation alone, with all higher functions founded in sensory experience, succinctly summarized in the axiom "to feel is to think" (Carr, 1930). In his 1754 "Treatise on the Sensations," Condillac used a hypothetical cognizant marble statue whose exterior could be opened one sense at a time and through which the perceptual consequences of each sensory system, either in isolation or combined with other senses, could be examined philosophically.

> For this purpose we imagined a statue constructed internally like ourselves, and animated by a mind which as yet had no ideas of any kind. We supposed the marble exterior of the statue to prevent the use of its senses, and we reserved to ourselves the right to open them at will to the different impressions of which they are susceptible. (Condillac, 1754, "Dedication to Madame la Comtesse de Vassé," xxxi)

Condillac's aim was to demonstrate that much of our experience and knowledge could be derived from a single sense. He first gave the statue a sense of smell and presented it with a rose. Without a concept of the external world or time, the statue's entire mental existence consisted of the rose's odor. A faint sensory echo of the odor remained as the rose was removed. With the presentation of a new smell, the statue sensed a change. With repeated exposure and practice, the sensory echoes developed into the faculties of memory and imagination, and the statue was able to compare and judge previous and present odors. Condillac went on to derive a range of faculties in a similar way, summarizing his argument as follows:

> Having proved that the statue is capable of attending, remembering, comparing, judging, discerning, imagining; that it has abstract ideas; that it has ideas of number and duration; that it knows general and particular truths; that it forms desires, expresses passions, that it loves, hates, wills; that it is capable of hope, of fear, and of wonder; and finally that it contracts habits; we must conclude that with one sense alone the understanding has as many faculties as with the five joined together. (Condillac, 1754, chap. 7, sec. 1)

Bonnet's "Analytical Essay on the Faculties of the Soul" was published in 1760, six years after Condillac's "Treatise on the Sensations." Bonnet's work is framed around the same statue man thought experiment but differs in two important respects. First Bonnet used his knowledge of the natural sciences to incorporate cerebral anatomy and function into his statue man. Second, and ironically, given that Condillac was the priest, Bonnet alone dealt with issues such as religion, the afterlife, and resurrection. Bonnet thus attempts a theory of an immortal soul, to be resurrected on the day of judgment, a substance he considered related to light and ether and linked to the corpus callosum through terminal nerve fibers or fluid within nerves themselves. However, Bonnet's soul had little part to play in sensation and cognition. His Law of Union stated:

> There are no sensations in the soul other than a consequence of movements operating in sensory nerve fibres, the Soul has to have something which corresponds to the play of these fibres. (Bonnet, 1782, sec. 686)

Thus movements in brain nerve fibers, in effect, held the same direct relation with sensory experience as the soul, and in this, Bonnet's use of the soul resonates with the contemporary concept of a neural correlate of consciousness—neural activity intimately linked to conscious experience even if the nature of the relationship remains uncertain. Without its religious connotations, Bonnet's soul is analogous to what might today be called mind: the sum of conscious perceptual, cognitive, emotional, and motor experience.

2.2 Bonnet's Neurobiology of Sensory Experience

Bonnet describes the sequence of events that follows presentation of a rose to the statue to illustrate the underlying mechanism of an isolated sensory experience.

> The infinitely small corpuscles that emanate from the rose form a scented atmosphere around it. They enter the nose through the air and agitate the nerve fibres that cover it. … The way in

which the scented corpuscles agitate the nerve fibres is unknown to me: I have no means of coming by this knowledge. … I think that the scented corpuscles, endowed with a certain movement and a certain degree of movement, communicate a certain portion of this movement to the branches of the olfactory nerve. … I do not know if the movement is a vibration, an undulation, pressure or any other movement I am able to imagine: I confine myself therefore to say in general that the scented corpuscles imprint a movement on the branches of the olfactory nerve. These branches pass to the brain and communicate to it a certain perturbation relative to that which they received from the object. I would be going beyond things if I pronounced on the manner by which these perturbations propagate to the brain. I have nothing but vague conjectures to offer my Reader below: for example, one could propose that the propagation operated by nervous fluid [is] akin to sound by the medium of air. One could also hypothesise that the perturbation propagates itself through the elementary components of the nerves, endowed perhaps with a certain activity by virtue of which they re-agitate one against another. I am not able to decide if the movement that the olfactory nerve imprints on the seat of the soul, or to be more precise, the part of the seat of the soul that corresponds to it, is the same movement in this region as in the nerve. Each part has its own manner of movement, corresponding to its structure. … It suffices me to say, like a principle or like a law of our being, that a certain movement of one or many nerves has a constant correspondence to a certain movement of one or many parts of the seat of the soul; and that a certain movement of one or many parts of the seat of the soul have constant correspondence to a certain movement of one or many nerves. The movement that the rose imprints on the olfactory nerve and which that transmits to the organ of sensation, causes that modification of the Soul that we experience as the term *the smell of the rose*. This modification is a *manner of being* of the soul, a state distinct from all other states. (Bonnet, 1782, secs. 38–45)

This excerpt highlights the neuroanatomical and neurophysiological foundations of Bonnet's theory. Replace "movement" with neural transmission and "soul" with "conscious experience," and one is left with a contemporary neuroscientific account. Bonnet's nerve fibers each carry a different sensation, different fibers for the smell of a rose and a carnation, for example, and different sets of fibers for vision, touch, and taste (Bonnet, 1782, sec. 85). Only the fibers related to vision result in the sensation of light; only those related to olfaction are associated with the sense of smell. Like Condillac, Bonnet examines the full range of experience in his statue man by adding further scents to that of a rose. Memory, pleasure, desire, attention, abstraction, passion, fatigue, imagery, the association of ideas, language, habit, surprise, love, and free will are accounted for in this way, each of these faculties grounded within his functional neuroanatomical model of vibrating nerve fibers and their relationships. The following examples illustrate his general approach: memory is the ability of a set of nerve fibers to retain and reactivate their particular pattern of movement; fatigue is the change in quality of an experience following prolonged vibration of a fiber; propagated vibrations from one fiber to another lead to associations of ideas; pleasure and beauty relate to the harmony of movement in different fibers; the abstraction of similar qualities in different sensations is based on similarities in the vibrations of their respective fibers.

2.3 Bonnet's Description of Visual Hallucinations

Bonnet is remembered by the clinical sciences for a few paragraphs hidden within chapter 23 of the "Analytical Essay." Here Bonnet argued that the mechanism of dreamed and waking sensory experience was identical, both relating to movements of nerve fibers. Connections between fibers formed sequences of ideas during wakefulness, and these connections also formed sequences of ideas during sleep; however, in sleep, fibers were activated by internal sensory events such as inputs from the digestive system, not external objects. A key point for Bonnet was that the sensation provoked by the movement of a nerve fiber was indifferent to whether the movement had been induced by an internal cause or an external object. Charles Lullin's visual hallucinations were introduced to illustrate this point further, although almost eighty years before Esquirol first used the term in a form recognized today,[1] Bonnet referred to his grandfather's experiences as visions. Bonnet argued that a vision occurred if, during wakefulness, nerve fibers were set in motion by something other than an external object. Visions lacked a sense of ownership because they occurred in the context of a logical train of thought that continued while the vision was present. Furthermore, the person experiencing the vision had no sense of control over the experience, was unable to make it go away by focusing attention on something else, and had no sense of being able to determine or alter the sequence of ideas within the vision.

The "Analytical Essay" contained only a brief summary of Lullin's experiences, mentioning visions of scaffolding and brickwork patterns; changes in the tapestries lining Lullin's apartment; and men, women, birds, carriages, and buildings. Bonnet emphasized that his grandfather was elderly, in good health, in particular without failing memory, and that he had impaired eyesight. For Bonnet, the hallucinations were both consistent with, and proof of, his functional anatomical model of the brain and its relation to perception:

> His brain was a theatre in which the machines executed scenes that surprised the spectator all the more for being entirely unanticipated. … It is not difficult to imagine physical causes that set in motion different fascicles of nerve fibres with sufficient force to represent to the soul the image of diverse objects with as much vividness as if the objects themselves agitated the fascicles. And if the fibres serving reflection are not themselves involved, if they remain in their natural state, the soul does not confuse the visions with reality in any way. (Bonnet, 1782, sec. 676)

The statue man, limited to the sense of olfaction, was capable of olfactory *visions* (Bonnet's italics) when nerve fibers were set in motion by some cause other than an external

1. Contemporary clinical use of the term is attributed to Jean Etienne Esquirol's definition of 1837.

scent; however, unlike Lullin, the statue man would be unable to distinguish hallucinations or dreams from reality, as it lacked the higher functions required. Turning to prophetic visions, Bonnet argued that God could prepare the brain of a prophet in such a way that a physical trigger at a predetermined time would set in motion a train of fibers allowing the prophet to experience a future event before it occurred.

2.4 Charles Bonnet Syndrome

Charles Lullin's hallucination diary was rediscovered in the late nineteenth century and published in full (Flournoy, 1902). Lullin's hallucinations are typical of those reported by patients with eye disease, and in honor of Bonnet's description, the association of visual hallucinations with eye disease is referred to today as the Charles Bonnet syndrome (CBS). CBS typically begins in the days and weeks following a significant decrease in vision. The hallucinations occur as a series of discrete episodes lasting seconds or minutes with, initially, many such episodes every day but a gradual reduction in their frequency over time. The visually rich and often bizarre nature of CBS hallucinations is illustrated in Lullin's descriptions presented in table 3.1. CBS hallucinations are silent, appear externally in the world, and are not under volitional control in the sense that the patient is unable to make them come or go or influence them by force of will, having the sense of being a spectator watching events enfold. Depending on the degree and extent of visual loss, real objects in the world will be blurred or not visually perceived. In contrast, hallucinations are seen in perfect detail. CBS patients invariably learn that such experiences are hallucinations; yet they may be so compelling that patients are often left uncertain of whether a given object is real or not. Many test the reality of such experiences, for example, by reaching out to touch them or assessing their plausibility.

3 The Visual Brain

What is happening in the brain during such experiences? Bonnet's philosophical view of specialized functional units underlying both normal perception and hallucinations has fared well in the era of brain imaging. Specialization for visual perceptual content is a core underlying principle of visual functional anatomy, not at the level of individual nerve fibers and their connections as conceived by Bonnet but at the level of cortical areas. Current understanding is that visual information passes from the eyes to the primary visual cortex (also referred to as striate cortex, V1 or area 17), a map of the visual world on the inner and polar surface of the occipital lobe in each cerebral hemisphere. Surrounding the primary cortex are repeated maplike representations specialized for different categories of visual perceptual content, specialization in this context meaning preferential responses to one category of content compared to another and not that the sole function of an area is to serve a single content category.

Table 3.1
Charles Lullin's visual hallucinations

Complex	Figures	Neatly dressed and coiffured ladies carrying a casket or an inverted table on their heads; young girls around 8 to 10 years old dressed in yellow silks with rose-colored ribbons, pearl collars, golden buckles, and diamond pendants, who danced around the room, one opening her mouth and showing her teeth; 18- to 20-year-old girls with Indian blue cloths and white bouquets and two well-dressed men of similar age to the girls, one with a red, the other with a gray, dress coat and hats bordered in silver. The figures were sometimes as tall as the ceiling. A man appeared every morning smoking a pipe identically dressed to Lullin with a cap and smoking jacket but whose face he could not see. Through his window, he hallucinated crowds in the street and three men in gray wearing hats advancing in a line into the street fountain.
	Objects	Carriage complete with driver and horses that expanded in correct proportion to the size of a house; ornate plates; an arch leading to a vaulted room with a picture of a landscape scene on the wall depicting a church; multiple pictures of different sizes in golden frames randomly placed on the walls from floor to ceiling; cranes for lifting heavy loads. The street fountain outside his window changed its shape and appeared to have a large column with a stone globe and two powerful jets of water.
	Animals	Pigeons of various sizes; flocks of larks and white fluttering butterflies.
	Faces	Although not mentioned by Lullin, patients with CBS often describe disembodied faces looming in front of them, often with feature distortions such as prominent eyes or teeth resulting in a grotesque or gargoyle-like appearance.
Simple	Shapes	Lullin's most frequent hallucinations were simple. These included a multitude of what Lullin referred to as atoms, varying in size and whirling about in his field of view; a blue handkerchief with four yellow circles with black borders in the corners and one in its center, whose size varied depending on where it was projected; spinning objects that reminded him of a component in an eighteenth-century weaving machine; a white satin sheet covered in black shapes with golden roses and circles. Sometimes the walls took on an orange tinge and were covered with pale blue, spinning, elongated, circular shapes about two inches long.
	Patterns	Walls of bluish cut stone with the line of mortar visible between the stones; scaffolding composed of an assortment of beams; off-white and golden clover patterns covering the walls and furniture; walls covered in antique books.

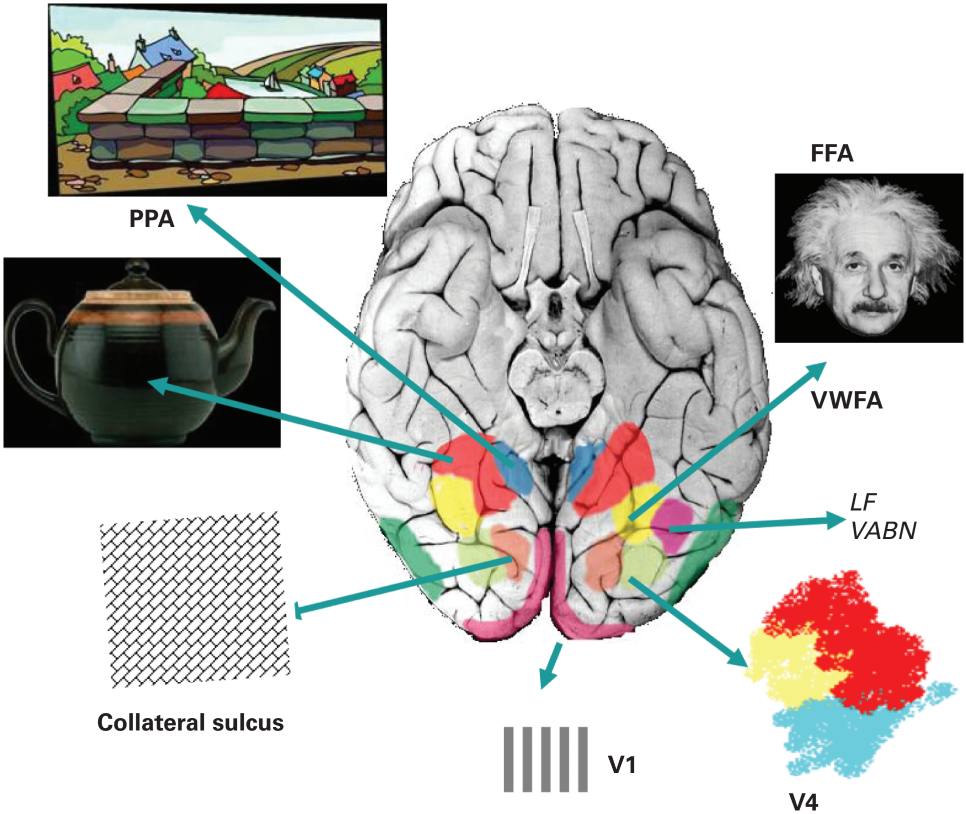

Figure 3.1
A ventral view of the brain with selected areas of relative specialization for different visual attributes. Specializations are shown (from bottom clockwise) for contrast, orientation, and luminance (V1); visual texture patterns; objects; landscapes (PPA = parahippocampal place area); familiar faces (FFA = fusiform face area); text and letter strings (VWFA = visual word form area); and colors (V4).

Figure 3.1 shows a selection of such specialized regions on the undersurface of the human brain extending from the occipital lobe to the undersurface of the temporal lobe. These areas are connected in complex ways through direct and indirect pathways whose detailed anatomy has yet to be determined. Specializations are found for familiar faces (Kanwisher, McDermott, et al., 1997), colors (Zeki, Watson, et al., 1991), extended landscapes (Epstein & Kanwisher, 1998), objects (Ishai et al., 1999; Bar et al., 2001), text and letter strings (Cohen, Dehaene, et al., 2000), and visual textures (Puce, Allison, et al., 1996). The lateral surface of the brain contains specializations for motion (Watson, Myers, et al., 1993), body parts (Downing, Jiang, et al., 2001), and eye and mouth movements (Puce, Allison, et al., 1998).

3.1 The Eye's Mind and Mind's Eye

The specializations described in the previous section have been identified by presenting visual stimuli of given content and comparing the magnitude of response in different brain regions. Selective increases in activity within a brain region indicate specialization for the content presented but leave open the question of whether such activity relates directly to the conscious experience of that content. The traditional view has been that activity in specialized visual cortex reflects unconscious visual processing, with the transition to consciousness occurring elsewhere in the brain. However, this seems an oversimplification. Brain imaging experiments designed to characterize correlates of visual consciousness suggest that activity in specialized visual cortex correlates with both unconscious and conscious vision (ffytche, 2002). What seems to differ in the conscious and unconscious states in these areas is the magnitude of response, perhaps reflecting differences in the type of processing or neural circuits involved in the two states (ffytche, 2002). For example, conscious perception of a face is associated with an increase in activity within face-specialized cortex compared to a nonconscious control stimulus, while conscious perception of a house or building is associated with increased activity in cortex specialized for spatially extended scenes (Moutoussis & Zeki, 2002). Similarly conscious perception of a faint visual grating is associated with an increase in activity within the primary visual cortex or regions in its immediate surrounds (Pins & ffytche, 2003). In the clinical domain, conscious perception of motion in the otherwise blind hemifield of a patient with a lesion of primary visual cortex (the Riddoch syndrome) is associated with an increase in activity within motion-specialized cortex (Zeki & ffytche, 1998). Such evidence indicates that at least part of the activity identified by functional brain imaging in specialized visual areas correlates with conscious visual perceptual experience; the view that it does so without necessity for further processing in higher or lower areas is termed the theory of microconsciousness (Zeki & Bartels, 1999). If we use the folk terminology of a *mind's eye* (the inner space in which we consciously experience visual imagery), activity in specialized visual cortex could be conceived as the *eye's mind*. In the *eye's mind*, visual experience becomes related to mind; in the *mind's eye*, mind becomes related to visual experience.

Brain imaging studies of visual imagery suggest that mind's eye and eye's mind involve different brain regions. During imagery the main areas of activation are in the frontal, parietal and medial temporal lobes, with little (Ganis, Thompson, et al., 2004) or absent (Howard, ffytche, et al., 1998) activation of specialized visual areas. Further evidence for a separation of brain regions serving eye's mind and mind's eye comes from patients with lesions of specialized visual cortex in whom eye's mind functions have been lost but mind's eye functions preserved (Bartolomeo, Bachoud-Levi, et al., 1997). The two broad domains of mind's eye and eye's mind are thus distinguishable both on the grounds that they each relate to different phenomenological spaces (the mind's eye to a spatially ill-defined inner world, and the eye's mind to the world around us) and on the grounds that they relate to spatially distinct sets of brain regions (the mind's eye to frontal, parietal and medial temporal cortex, the eye's mind to specialized visual cortical regions).

4 The Neurobiology of Visual Hallucinations

Which of the two domains is linked to visual hallucinations? We have been able to answer this question by using brain imaging techniques to study patients with CBS hallucinations while they hallucinate (ffytche, Howard, et al., 1998). Patients lay in the scanner and indicated the onset and offset of their hallucinations with a button press, allowing us to identify brain regions in which activity changed at the time of a hallucination. Activity changes invariably occurred within eye's mind, not mind's eye, regions, the content of a hallucination relating to the specialization of the eye's mind region activated. Thus if activity increased in color-specialized cortex, the patient hallucinated colors; if in object-specialized cortex, the patient hallucinated objects; and if in face-specialized cortex, the patient hallucinated faces (ffytche, Howard, et al., 1998). Since the patients were visually impaired, we had to rely on published coordinates from studies of normal-sighted subjects to identify the relevant cortical specializations. However, more recently the link between cortical specialization and hallucination content has been confirmed using a patient with schizophrenia where follow-on specialization studies could be performed (Oertel, Rotarska-Jagiela, et al., 2007). In this patient, the specialization of eye's mind regions activated during hallucinations matched the content of the hallucinations, just as in CBS. However, in the schizophrenia patient, brain regions associated with memory also seemed to be involved, an issue I return to later.

Whether the relationship between cortical specialization and hallucination content is also true of hallucinations in other sensory modalities is less clear, partly because of our limited understanding of the cortical organization of higher auditory, tactile, olfactory, and gustatory function. However, it seems likely that the same principle will apply as hallucinations in these modalities are linked to cortical activation within their respective sensory systems (see ffytche, 2008).

What causes eye's mind cortex to spontaneously activate in CBS? Bonnet referred to unspecified physical causes, and in some respects, our understanding of the phenomenon has advanced little beyond this. Current thinking is that the spontaneous activity is caused by loss of visual input. An early version of this theory was developed by psychiatrist Louis Jolyon West in the 1950s and held that a constant stream of background processing and redundant sensory input was kept outside the sphere of consciousness by a process conceived in terms of scanning, filtering, and inhibiting. Loss of sensory input altered this process and, in so doing, *released* redundant information that appeared in the conscious realm given a sufficient level of cortical arousal.

West provided the analogy of a man looking out of a window from a room containing a fire. In bright sunlight (analogous to sensory input), the man sees only the world outside; however, as night begins to fall, the man begins to see things inside the room reflected on the glass. While the fire burns brightly (analogous to cortical arousal), the man sees the contents of the room as if they were outside the window, but when the fire dies down he sees nothing. This account is referred to today as the *release* theory of visual hallucinations, and although flawed in neurophysiological detail (visual inputs are not predominantly inhibitory, for example), the principle turns out to be correct. Retinal lesions in animal models reduce activity in some parts of the visual cortex but lead to sustained increases in spontaneous activity and visual responses in others (Eysel, Schweigart, et al., 1999). These increases in activity are the result of decreases in inhibition mediated by the neurotransmitter GABA and increases in excitation mediated by the neurotransmitter glutamate (Eysel, Schweigart, et al., 1999). The neurophysiological revision of release theory is referred to as the *deafferentation* theory of visual hallucinations (Burke, 2002).

4.1 Hallucinations in Relation to Other Visual Perceptual Phenomena

Our understanding of the nature of hallucinations and their relation to other types of perceptual experience is based on philosophical, introspective, experimental, and clinical distinctions, each tradition deriving its own classificatory scheme. However, neuroimaging provides the opportunity to approach all such phenomena from a novel perspective, allowing us to ask in what way brain activity during hallucinations is similar or different to that found in other perceptual states. Figure 3.2 presents a number of visual perceptual experiences laid out on three axes. One axis relates to the perceptual locus of a given type of experience (external in the visual world: left of the figure; internal in the mind's eye: right of the figure). Another axis relates to the sense of agency or volitional control the subject has over the type of experience (full volition, under control of the subject: top of the figure; no volition, subject a spectator: bottom of the figure). A third axis relates to the vividness of the experience (vague: behind the figure; hyperintense: in front of the figure). Although the figure focuses on visual experience, a similar representation could be derived for perceptual phenomena in any of the senses. The experience of seeing a real (mind-independent) object in the world around us (referred to here as normal perception) provides a reference point from which to compare other experiences. Visual hallucinations, whether complex, simple, or recognized as a hallucination or not,[2] visual illusions, visual dreams, and visual afterimages are all located externally and are devoid of a sense of agency but vary in terms of their vividness. For example, visual hallucinations of color

2. The term "pseudohallucination" is used by some psychiatric traditions to refer to hallucinations that are recognized as hallucinations.

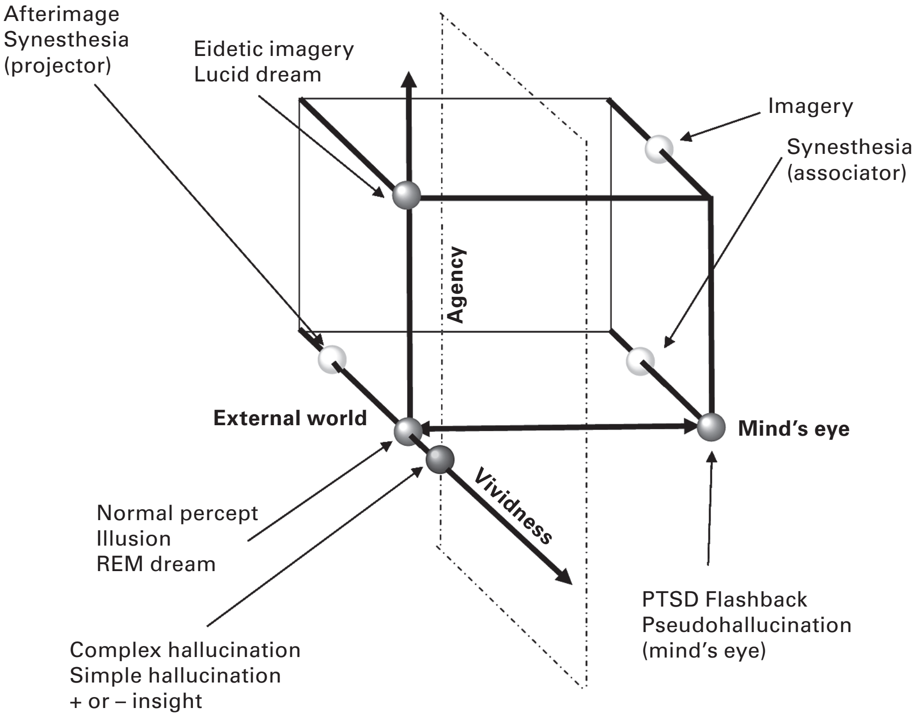

Figure 3.2
The neurophenomenological classification of visual perceptual experience. A three-dimensional space is represented with axes: (i) perceptual locus (external or in the mind's eye), (ii) sense of agency or volitional control, (iii) vividness (also coded by saturation). Each category of visual perceptual experience is represented by a sphere. The dotted vertical plane divides experiences related predominantly to activity in the specialized visual cortex of the eye's mind (left of figure) from experiences related predominantly to activity in parietal, frontal and medial temporal regions of the mind's eye (right of figure).

are often described as hyperintense (hyperchromatopsia; see ffytche & Howard, 1999), while afterimages are typically vague. Visual imagery appears in the mind's eye and is entirely under volitional control. Eidetic imagery, today perhaps better known as photographic memory, consists of vivid afterimages seen in the same colors as the original stimulus (unlike the complementary colors of normal afterimages) and are under the control of the imager, who can evoke the experiences at will. Lucid dreams are external and vivid but, unlike normal dreams, have a sense of self and agency in controlling the narrative. Post-traumatic stress disorder (PTSD) flashbacks lack a sense of agency and, although all-enveloping and vivid, occur in the mind's eye. When occurring without obvious link to previous traumatic events, experiences similar in other respects to PTSD flashbacks are classified as a variant of normal imagery.[3] In synesthesia, stimulus content of one type induces simultaneous experiences of another, either within the same sensory domain or crossing sensory domains (e.g., letter stimuli inducing color experiences or sound experiences inducing colors). The synesthetic experiences lack a sense of agency but fall into two categories, one experienced externally in the world (projector synesthetes), the other in the mind's eye (associator synesthetes) (Dixon, Smilek, et al., 2004).

The phenomenological space illustrated in figure 3.2 is complex and populated by a range of visual perceptual categories defined by philosophical, clinical, or experimental criteria. For example, illusions are held distinct from hallucinations on philosophical grounds of a difference in their relationship to external objects, present in an illusion and absent in a hallucination. Similarly, hallucinations recognized as hallucinations or mistaken for reality (with and without insight in clinical terminology) are held as distinct based on different prognostic implications, those without insight suggestive of certain mental disorders. Yet the complexity of figure 3.2 collapses to a simple dichotomy when viewed from the neurophenomenological perspective of brain imaging (see ffytche, 2005, 2007). The predominant brain activation associated with experiences to the left of the dotted vertical plane (perceived externally) lies within the specialized visual areas of the eye's mind, while the predominant brain activation associated with experiences to the right of the vertical plane (perceived in the mind's eye) lies within frontal, parietal and medial temporal regions. Thus a percept of motion (Zeki & ffytche, 1998), an illusion of motion (Zeki, Watson, et al., 1993), and an afterimage of motion (Tootell, Reppas, et al., 1995) are all linked to activity within the eye's mind cortical region specialized for motion. Hallucinations of motion are likely to activate the same motion-specialized cortex, although they have yet to be captured in brain imaging experiments. In contrast, imagery of motion involves activation predominantly within mind's eye regions of the frontal lobe (Binkofski, Amunts, et al., 2000).

The collapse of phenomenological space into two regions related to activity in either the eye's mind or mind's eye is, of course, a simplification. Brain imaging can at best only provide a crude macroscopic view of changes in activity and not details of the underlying circuitry or processing. Activation in a given brain region associated with different categories of experience may, on closer inspection, turn out to reflect entirely different processes. Yet it would seem reasonable to suppose that activation of a single brain region across two categories of experience indicates a closer relationship between categories than would be the case if each was associated with activity in a different brain region. Conversely, the activation of different brain

3. The term "pseudohallucination" is used by some psychiatric traditions to refer to involuntary visual imagery. Confusingly this use of the term is entirely different to that outlined in note 2.

regions across two categories of experience is likely to indicate that the experiences are of a different nature. This is not meant to imply that hallucinations of color are a different category of experience from hallucinations of visual motion by virtue of their respective associations with color- and motion-specialized cortex. The key border defining experiential category is that dividing the cortical territories of the eye's mind and mind's eye. Thus, despite sharing visual motion content, a hallucination of visual motion is a different category of experience from imagery of visual motion by virtue of its association with the eye's mind as opposed to the mind's eye cortex.

5 The Nature of Hallucinations

The neurophenomenological taxonomy derived in the previous section carves categories of visual perceptual experience in a way that differs from classifications based on introspective, clinical, experimental, and philosophical approaches. Experiences that are distinct in previous classificatory schemes become closely related within the neurophenomenological framework, while experiences that were closely related become distinct.

5.1 Charles Bonnet Syndrome Hallucinations as Generic Perceptual Representation

From Bonnet to the modern era, visual hallucinations have been conceived as visual memories that have been inappropriately reactivated through a mechanism that varies from theory to theory. In the psychoanalytic tradition, the reactivation is conceived in terms of redirected internal drives; in release theory, it is conceived in terms of loss of inhibition to background memory processing. Such theories would predict that CBS hallucination content would be clearly associated with past experience, yet where this issue has been specifically addressed, little evidence has emerged to support it. Teunisse et al. found that 77 percent (46/60) of the CBS patients surveyed found no personal relevance of their hallucinations (Teunisse, Cruysberg, et al., 1996). One patient even noted that her visual hallucinations carried less personal relevance than her dreams. The implication is that patients are not hallucinating visual memories in the sense of visual content encountered previously; indeed, much of the bizarre content reported could not have been encountered. The imaging evidence supports this view. Visual memory as measured by visual imagery is not closely linked to eye's mind territory, as pointed out earlier. That eye's mind activity underlies CBS hallucinations argues strongly against visual memories as the source of CBS hallucination content. CBS visual hallucinations seem better conceived as generic representations or visual processes underlying normal visual function. The type of representations and processes envisaged are illustrated by the face-processing network. Although a seemingly unitary function, the perception of a face involves several brain regions, some extracting face features, others face wholes, and yet others face-related social signals such as eye gaze and mouth movements (Haxby, Hoffman, et al., 2000). It is the processes and representations embodied in different subregions of this network that seem to underlie the content of CBS face hallucinations. Thus face hallucinations are not of remembered familiar faces, as would be expected if hallucinations were reactivated memories, but of isolated features, faces dominated by features (as described in table 3.1), or faces with fixed gaze or silent gaping mouths. Other classes of hallucination, for example, figures in period costume wearing elaborate headgear, are likely to reflect representations and processing functions within different networks, although the details are at present unclear.

The generic template and processing account suggests that CBS hallucination content is based on juxtaposed or unusually intense fragments of normal visual perception. Impossible objects or percepts of properties never previously encountered should not occur. Whether this prediction is correct will require further study; however, my clinical experience is that it is. Hallucinated colors are typically described as more vivid than their real counterparts (hyperchromatopsia; see ffytche & Howard, 1999), yet I have not encountered patient descriptions of entirely novel hues.

5.2 Blurring the Boundaries of Hallucinations

One consequence of the neurophenomenological classification presented here is the blurring of traditional boundaries between perceptual categories. For example, from a philosophical perspective, illusions and hallucinations are classified as distinct; illusions, but not hallucinations, are linked to an external object. Similarly in the clinical domain, illusions are classified as distinct from hallucinations by virtue of a weaker association with mental illness. However, such categorical boundaries begin to appear less absolute when confronted with real clinical cases. Illusions and hallucinations typically co-occur within the same patient, and it is often difficult to categorize pathological visual experiences as either one or the other category.[4] Such practical difficulties hint at the deeper problem revealed by imaging evidence. From the neurobiological perspective, hallucinations and illusions are more similar than different, both related to activity within the cortical territory of the eye's mind. If hallucinations and illusions are the same category of phenomena, the issue arises as to whether they each require a different theoretical account. The same issue applies to differences between hallucinations, dream states, and normal visual percepts. One might argue that instead of a

4. Polyopia is an example of a pathological visual perceptual experience that can equally be classed hallucination or illusion. Multiple copies of a real object or object feature occur simultaneously, the copies typically aligned as a geometrical pattern. Since a real object is present, the experience can be considered an illusion. Alternatively the copies of the object can be considered multiple hallucinations.

theory specific to hallucinations, we should be aiming for a theory that encompasses all eye's mind phenomena.

5.3 Fragmenting Hallucinations

Current accounts of hallucinations treat them as a single class of perceptual entity; however, evidence is emerging in the visual domain that this may not be the case (ffytche, 2007). When viewed across the spectrum of clinical conditions in which visual hallucinations occur, three distinct but overlapping sets of hallucination contents emerge (visual hallucinatory syndromes). One is CBS as described earlier, found in conditions where neural input to the visual cortex is lost through eye or visual pathway disease. The second is linked to ascending brain stem neurotransmitter dysfunction, particularly in the cholinergic system (Perry & Perry, 1995). In these conditions, simple hallucinations such as the patterns found in CBS do not occur. Instead visual hallucinations are typically of figures or animals, occur in association with hallucinations in other modalities, and are often associated with false beliefs concerning their cause (delusions). The third syndrome is linked to alterations of serotonergic function. Here patients describe illusions, typically persistent afterimages and image trails, and simple but not complex visual hallucinations. Patients with one syndrome rarely develop another, suggesting that each is a distinct clinical entity related to dysfunction within a different class of neural inputs. Thus visual hallucinations might be caused by deafferentation of the visual system in one patient, loss of cholinergic inputs in another, and serotonergic dysfunction in a third. The challenge to our current view of hallucinations is that each of these neurophysiological mechanisms requires a different type of theory. Cholinergic inputs are linked to arousal, memory, and dreaming and lead to a very different type of theoretical account to that based on visual processing and generic feature analysis proposed earlier for CBS. A theory of hallucinations based on serotonergic function would be different again. An illustration of these differences has already been alluded to in the finding that brain regions linked to memory are involved in the visual hallucinations of schizophrenia but not CBS. Thus even within the visual domain, hallucinations cannot be treated as a single perceptual category or accounted for by a single theory. There are likely to be several categories of hallucination, each with a different neurobiological basis. Whether these categories are distinguishable on phenomenological grounds or translate to different sensory and motor modalities remains to be determined. However, it is clear we require more than one theory of hallucinations.

6 Conclusions

Brain imaging advances of the last decade have provided a novel perspective to challenge our preconceptions of the nature of visual hallucinations. Brain activity forces us to reconsider where hallucinations sit in relation to other perceptual phenomena and their future as a unitary category. What visual hallucinations will become is at present unclear. The natural classes of eye's mind and mind's eye phenomena seem a useful starting point from which to build future accounts; however, it is not at present obvious how the different neurophysiological categories of eye's mind phenomena might be distinguished and whether they generalize beyond the visual domain. Bonnet was not troubled by distinctions between hallucinations, illusions, and normal perception; his philosophical neurophysiology of *visions* emphasized the neural substrate common to such phenomena almost eighty years before their current taxonomic boundaries were imposed. Given the emerging neurobiological challenges, it may yet be that Bonnet's account survives long after the era of hallucinations as we know them today has passed.

References

Bar, M., Tootell, R. B., Schacter, D. L., Greve, D. N., Fischl, B., Mendola, J. D., et al. (2001). Cortical mechanisms specific to explicit visual object recognition. *Neuron*, *29*(2), 529–535.

Bartolomeo, P., Bachoud-Levi, A. C., & Denes, G. (1997). Preserved imagery for colours in a patient with cerebral achromatopsia. *Cortex*, *33*, 369–378.

Binkofski, F., Amunts, K., Stephan, K. M., Posse, S., Schormann, T., Freund, H. J., et al. (2000). Broca's region subserves imagery of motion: A combined cytoarchitectonic and fMRI study. *Human Brain Mapping*, *11*, 273–285.

Bonnet, C. (1782). *Oeuvres d'histoire naturelle et de philosophie de Charles Bonnet* (Vols. 13–14): *Essai analytique sur les facultés de l'ame*. (Facsimile edition, 2006, Elibron Classics.) Neuchatel: Samuel Fauche.

Burke, W. (2002). The neural basis of Charles Bonnet hallucinations: A hypothesis. *Journal of Neurology, Neurosurgery, and Psychiatry*, *73*, 535–541.

Carr, G. (1930). *The life and works of Condillac: Condillac's* Treatise on the sensations. London: Favil Press.

Cohen, L., Dehaene, S., Naccache, L., Lehéricy, S., Dehaene-Lambertz, G., Hénaff, M., et al. (2000). The visual word form area: Spatial and temporal characterisation of an initial stage of reading in normal subjects and posterior split-brain patients. *Brain*, *123*, 291–307.

Condillac, E. B. (1754). *Treatise on the sensations* (Carr, G., Trans.). London: Favil Press.

Dixon, M. J., Smilek, D., & Merikle, P. M. (2004). Not all synaesthetes are created equal: Projector versus associator synaesthetes. *Cognitive, Affective, and Behavioral Neuroscience*, *4*, 335–343.

Downing, P. E., Jiang, Y., Shuman, M., & Kanwisher, N. (2001). A cortical area selective for visual processing of the human body. *Science*, *293*, 2470–2473.

Epstein, R., & Kanwisher, N. (1998). A cortical representation of the local visual environment. *Nature*, *392*, 598–601.

Eysel, U. T., Schweigart, G., Mittmann, T., Eyding, D., Qu, Y., Vandesande, F., et al. (1999). Reorganization in the visual cortex after retinal and cortical damage. *Restorative Neurology and Neuroscience*, *15*, 153–164.

ffytche, D. H. (2002). Neural codes for conscious vision. *Trends in Cognitive Sciences*, *6*, 493–495.

ffytche, D. H. (2005). Visual hallucinations and the Charles Bonnet syndrome. *Current Psychiatry Reports*, *7*, 168–179.

ffytche, D. H. (2007). Visual hallucinatory syndromes: Past, present, and future. *Dialogues in Clinical Neuroscience*, *9*, 173–189.

ffytche, D. H. (2008). The hodology of hallucinations. *Cortex*, *44*, 1067–1083.

ffytche, D. H., & Howard, R. J. (1999). The perceptual consequences of visual loss: Positive pathologies of vision. *Brain*, *122*, 1247–1260.

ffytche, D. H., Howard, R. J., Brammer, M. J., David, A., Woodruff, P., & Williams, S. (1998). The anatomy of conscious vision: An fMRI study of visual hallucinations. *Nature Neuroscience*, *1*, 738–742.

Flournoy, T. (1902). Le cas de Charles Bonnet: Hallucinations visuelles chez un vieillard opéré de la cataracte. *Archives de Psychologie*, *1*, 1–23.

Ganis, G., Thompson, W. L., & Kosslyn, S. M. (2004). Brain areas underlying visual mental imagery and visual perception: An fMRI study. *Cognitive Brain Research*, *20*, 226–241.

Haxby, J. V., Hoffman, E. A., & Gobbini, M. I. (2000). The distributed human neural system for face perception. *Trends in Cognitive Sciences*, *4*, 223–233.

Howard, R. J., ffytche, D. H., Barnes, J., Mckeefry, D., Ha, Y., Woodruff, P. W., et al. (1998). The functional anatomy of imagining and perceiving colour. *Neuroreport*, *9*, 1019–1023.

Ishai, A., Ungerleider, L. G., Martin, A., Schouten, J. L., & Haxby, J. V. (1999). Distributed representation of objects in the human ventral visual pathway. *Proceedings of the National Academy of Sciences of the USA*, *96*(16), 9379–9384.

Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: A module in human extrastriate cortex specialised for face perception. *Journal of Neuroscience*, *17*, 4302–4311.

Locke, J. (1690/1961). *An essay concerning human understanding*. Ed. J. W. Yolton. London: Dent.

Moutoussis, K., & Zeki, S. (2002). The relationship between cortical activation and perception investigated with invisible stimuli. *Proceedings of the National Academy of Sciences of the USA*, *99*, 9527–9532.

Oertel, V., Rotarska-Jagiela, A., van de Ven, V. G., Haenschel, C., Maurer, K., & Linden, D. E. (2007). Visual hallucinations in schizophrenia investigated with functional magnetic resonance imaging. *Psychiatry Research: Neuroimaging*, *156*, 269–273.

Perry, E. K., & Perry, R. H. (1995). Acetylcholine and hallucinations: Disease-related compared to drug-induced alterations in human consciousness. *Brain and Cognition*, *28*, 240–258.

Pins, D., & ffytche, D. H. (2003). The neural correlates of conscious vision. *Cerebral Cortex*, *13*, 461–474.

Puce, A., Allison, T., Asgari, M., Gore, J. C., & McCarthy, G. (1996). Differential sensitivity of human visual cortex to faces, letterstrings, and textures: A functional magnetic resonance imaging study. *Journal of Neuroscience*, *16*, 5205–5215.

Puce, A., Allison, T., Bentin, S., Gore, J. C., & McCarthy, G. (1998). Temporal cortex activation in humans viewing eye and mouth movements. *Journal of Neuroscience*, *18*, 2188–2199.

Teunisse, R. J., Cruysberg, J. R., Hoefnagels, W. H., Verbeek, A. L., & Zitman, F. G. (1996). Visual hallucinations in psychologically normal people: Charles Bonnet's syndrome. *Lancet*, *347*, 794–797.

Tootell, R. B. H., Reppas, J. B., Dale, A. M., Look, R. B., Sereno, M. I., Malach, R., et al. (1995). Visual motion aftereffect in human cortical area MT revealed by functional magnetic resonance imaging. *Nature*, *375*, 139–141.

Watson, J. D. G., Myers, R., Frackowiak, R. S. J., Hajnal, J. V., Woods, R. P., Mazziotta, J. C., et al. (1993). Area V5 of the human brain: Evidence from a combined study using positron emission tomography and magnetic resonance imaging. *Cerebral Cortex*, *3*, 79–94.

Zeki, S., & Bartels, A. (1999). Toward a theory of visual consciousness. *Consciousness and Cognition*, *8*, 225–259.

Zeki, S., & ffytche, D. H. (1998). The Riddoch syndrome: Insights into the neurobiology of conscious vision. *Brain*, *121*, 25–45.

Zeki, S., Watson, J. D. G., & Frackowiak, R. S. J. (1993). Going beyond the information given: The relation of illusory visual motion to brain activity. *Proceedings of the Royal Society of London, Series B: Biological Sciences*, *252*, 215–222.

Zeki, S., Watson, J. D. G., Lueck, C. J., Friston, K. J., Kennard, C., & Frackowiak, R. S. J. (1991). A direct demonstration of functional specialization in human visual cortex. *Journal of Neuroscience*, *11*, 641–649.