

A Cognitive Neuroscience of Alzheimer's Disease: What Can Be Learned from Studies of visual Imagery?

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Summary

Complex cognitive abilities are subserved by sets of component subsystems working together. Behavioral deficits, such as those that occur in Alzheimer's disease, arise when subsystems malfunction or interact improperly. A theory of component subsystems of visual mental imagery is described, which specifies five major sets of components; these components are hypothesized to be implemented in different regions of the brain. The theory is used to guide investigations of the effects of normal aging on different aspects of imagery, and the results of these studies suggest that normal aging selectively affects aspects of imagery that depend on frontal lobe function. These findings are used to formulate hypotheses about possible relations between Alzheimer's disease, normal aging, and visual mental imagery.

Introduction

Cognitive functions break down selectively following a brain disorder, whether due to a focal injury such as a stroke, or more diffuse degeneration, such as Alzheimer's disease. The precise way functions break down depends on the structure of normal cognitive mechanisms. In this chapter we briefly consider a theory of the major components of visual mental imagery, and consider the implications of this architecture for understanding some aspects of normal aging and Alzheimer's disease.

The theory we summarize here was formulated within the perspective of cognitive neuroscience. This approach to visual imagery led us to provide a description of information processing that rests on facts about the neural underpinnings of vision. We assume that complex cognitive abilities arise when different sets of component subsystems interact. Each such component carries out a single type of mapping between an input and output.

Components of Visual Imagery

It has long been known that visual mental imagery relies on some of the same mechanisms that are used in visual perception (for a good review of evidence,

see Farah 1988). This is salubrious, given that we know a great deal about visual perception. Thus, we can gain a leg up on a theory of imagery by considering perception. In this section we provide a brief overview of the major features of the visual system, focusing on those aspects that involve stored information (so-called "high level" visual processes; for a more detailed treatment, see Kosslyn et al. 1990; Kosslyn 1991).

Visual Buffer

Introspectively, visual mental images appear to embody spatial properties of objects and scenes. For example, consider what seems to occur when you try to answer questions such as: "Which is longer, a donkey's ears or an ear of corn?" "Which is darker green, a Christmas tree or a frozen pea?" "Which is wider, a lightbulb or a tennis ball?" Most people report that they visualize the objects, and "see" the necessary properties. This sort of introspection suggests that visual mental images reconstruct the spatial properties of an object.

And in fact, numerous areas of cerebral cortex are spatially organized; patterns of activity within these areas make explicit the spatial organization of a stimulus. During visual perception, these areas represent images by mirroring the pattern of activation on the retina, and hence these areas are said to be "retinotopically organized." For example, Tootell et al. (1982) used a 2-deoxy-D-glucose (2DG) method to study the retinotopic organization of visual areas in Macaque monkeys. The monkeys were trained to stare at a flashing pattern and then were injected with a dose of 2DG. The more a given neuron worked when the monkey was staring at the pattern, the more of this radioactively tagged sugar it took up. After the animal stared at the pattern for 25–30 min, it was sacrificed and the pattern of radioactivity in its brain was examined. The radioactive trace of the sugar consumed by cortical nerve cells produced a pattern in area V1 (at the posterior end of the occipital lobe) that mirrored the actual pattern itself; it was as if there was a picture of the pattern laid across this area of cortex. Felleman and van Essen (1991) estimate that at least 15 cortical areas of the Macaque monkey have this type of spatial organization.

Fox et al. (1986) used positron emission tomography (PET) to show that area V1 in humans is also retinotopically organized. This is of interest because Kosslyn et al. (1991) showed that this area is active during visual mental imagery. Thus, we can infer that at least some of the spatial properties of visual mental imagery may arise when spatial patterns are activated from memory, not from the eyes, in spatially organized regions of cortex. We call these regions the "visual buffer."

Attention Window

There is far more information in the visual buffer than can be processed in detail. Thus, it is of interest that there appears to be an "attention window" within this

buffer, which selects a region of the patterns of activity in the visual buffer and sends it to other areas for further processing (cf. Moran and Desimone 1985; Treisman and Gelade 1980).

Encoding Object Properties Versus Spatial Properties

The information within the attention window is further processed in two different pathways. One pathway goes from V1 ventrally to the temporal lobe, while the other pathway goes dorsally to the parietal lobe. To investigate what is processed in each pathway, Ungerleider and Mishkin (1982; see also Pohl 1973) trained Macaque monkeys to use either object properties or spatial information to find food. Different parts of the animal's brain were removed after the task was learned, and the behavioral deficits were observed. Removal of the temporal and parietal lobes resulted in a double disassociation: ablating the temporal lobes drastically affected an animal's ability to encode shape, but did not have much of an effect on its ability to encode location; in contrast, ablating the parietal lobes had the opposite effect. These results suggest that the dorsal pathway acts as a spatial encoding subsystem, whereas the ventral pathway acts as an object properties encoding components subsystem. Consistent with these inferences, neuroanatomical and neurophysiological studies have found neurons that are sensitive to shape and color in the temporal lobes (Desimone et al. 1984; Gross et al. 1984), and location and motion in the parietal lobes (Hyvarinen and Poranen 1974; Mountcastle et al. 1975; Anderson et al. 1985).

The division between encoding object properties (color and texture, in addition to shape) and spatial properties (size and orientation, in addition to location) makes sense from a computational point of view. Rueckl et al. (1989) trained a neural network computer model to distinguish between nine different shapes, each in nine different positions. A three layer feedforward network was used, which consisted of an input layer of 25 units (representing a 5×5 input matrix), a hidden layer of 18 units, and an output layer of 18 units; nine of the output units indicated the input shape (one unit per shape), and nine indicated the location (one unit per location). In one version of the model, all of the hidden units were connected to all of the output units; in another version, some of the hidden units were connected only to the output units that indicated shape, and the others were connected only to the output units that indicated location. Splitting processing into two distinct streams properly resulted in much better performance than having all functions take place in a single, undifferentiated system.

The split networks did especially well when more resources were allocated to the 'what' task (14 of 18 units); this finding suggests not only that the 'what' and 'where' functions are computationally distinct, but also that identifying shapes is computationally more demanding than registering location – and in fact there are more neurons in the temporal object-properties system than in the parietal spatial-properties system (e.g., see van Essen 1985).

If visual memories reside in the object-properties system in the temporal lobe, as some have argued (for a review, see Kosslyn 1991), then visual images might be formed by activating these memories. This idea is plausible in part because the neural connections from lower-level visual areas to higher-level ones are reciprocal; they run in both directions. Thus, activating a visual memory in the temporal lobes could evoke a spatial pattern in the lower-level retinotopically organized areas. One reason that this would be necessary is that the higher-level visual areas in the temporal lobe are not spatially organized; thus, to reconstruct the spatial properties of objects, activity must be induced in lower-level, retinotopically mapped areas.

Associative Memory

The object- and spatial-properties encoding systems send information into the frontal lobe, which appears to have special short-term memories for different types of sensory input (Goldman-Rakic 1987). Furthermore, we can infer that there must be a long-term memory representation (probably not in the frontal lobes) that associates object properties with spatial properties; the mere fact that people can recall where furniture is located in their homes indicates that the two sorts of information must have been conjoined. This memory representation is multimodal, associating not only simply visual object properties and spatial properties, but also auditory, tactile, and other sorts of information.

This long-term memory representation is relevant to imagery in part because many complex objects are encoded over the course of numerous eye movements. In this case, parts may be encoded separately, and a representation of the structure of the object (indicating how parts are spatially organized) would be stored in associative memory. If so, then when such an object is visualized, this structure would be accessed to find the locations where the parts should be visualized.

Top-down Processing

During visual object identification, one sometimes cannot identify an object at first glance; the information encoded in a single eye fixation is not sufficient to match a stored representation. However, the input provides some indication of what is being viewed, and the partial match to stored representations may serve as a hypothesis. In this case, additional information is needed to make the identification. Frontal lobe processes apparently access information in associative memory and use this information to guide further eye fixations; area 8 of the frontal lobes (also known as the frontal eye fields) plays a major role in guiding eye movements, and many have found that damage to the frontal lobe disrupts systematic search (e.g., Luria 1980).

When visual mental images are formed, these processes access the stored representation of the structure of an object in associative memory and send information to the temporal lobes to activate images of the individual parts; the

stored representation of spatial relations among the parts leads the system to form the image at the correct relative location for a part, so that the composite image is built up sequentially over time (for further details, see Kosslyn 1991). Kosslyn et al. (1988) provide evidence that images are in fact built up part-by-part over time.

Effects of Age on Imagery

We used our conception of imagery processing to guide investigations of the effects of increased age on visual mental imagery. Our approach to imagery suggests that a complex system forms and uses images, and some components are involved in some aspects of imagery but not others. Thus, we expected any factor that selectively affects components of the system to selectively affect different aspects of imagery.

Visual mental imagery, like other complex abilities, is not unitary and undifferentiated. Rather, it is useful to conceive of imagery as four distinct abilities. Consider the following task: you are loading luggage into the trunk of your car. You first study the pile on the curb, and then turn and visualize one suitcase in the trunk, and then another, and another. You imagine turning the suitcases, trying to fit them optimally into the trunk. While you are imaging placing one suitcase, you hold the images of the others where they seem best placed.

This task illustrates the four abilities, as follows. First, you had to *generate* an image of the suitcases; this involves activating visual memories. You not only activated the representations of shapes, causing a spatial pattern of activity in retinotopically mapped areas, but you also may have used stored descriptions in associative memory to help you arrange the shapes. For example, if you had packed those bags before, you might know that the big one nestles nicely against one side of a smaller one and fits nicely next to the spare tire; this information is used to direct where the images should be formed in the visual buffer.

Second, you had to *inspect* the image, scanning around and “seeing” whether the suitcases were properly placed; this involves shifting the attention window and encoding objects in the image – just as you would encode objects you see during perception. Thus, the object properties system is used both to form the image and then to match the subsequent input to visual memories, allowing you to recognize patterns that may have been only implicit in the image. For example, if asked if a cat has curved front claws, you might visualize the claws and then match the image to representations of curved vs. straight claws; never having thought about this before, you did not have an explicit representation of this property, but it was implicit in the image.

Third, you mentally *transform* objects in the image, moving them around; this function appears to involve parietal lobe and frontal lobe structures (Deutsch et al. 1988). Kosslyn (1987) suggests that the parietal lobes may be involved in shifting the location representation, but that this process is noisy; frontal lobe processes are involved in accessing information that is used to “clean up” the image. Thus, objects in images are transformed in small steps (see Shepard and

Cooper 1982), partly so that errors due to noisy shifting processes can be corrected before they are compounded.

Finally, as you scanned and transformed the objects in the image, you had to *maintain* the composite image. This process presumably involves repeatedly activating the visual memory in the temporal lobes, but does not require repeatedly accessing long-term associative memory. Maintaining an image can be achieved by re-encoding the image into the object properties system (as is done in visual perception), and then "bouncing" the pattern back into the visual buffer. Depending on how the imaged pattern is re-encoded, it will be more or less easily visualized; if one encodes it as relatively few perceptual units, less processing will be required than if one encodes it as relatively many perceptual units, each of which must be activated individually.

We examined the effects of age on these four abilities in young and old subjects (for a detailed report, see Dror and Kosslyn 1991). One group included 16 young subjects with an age range of 18–23 years (with a mean age of 20 years), and the other group included 16 elderly subjects with an age range of 55–70 years (with a mean age of 63 years). Each subject was tested on four tasks.

The first task tapped onto the image generation processes component. In this task the subjects were asked to generate an image of an uppercase letter within a set of four brackets placed at the vertices of an otherwise invisible rectangle. The subjects were to compare the imaged letter to a small "x" mark that was placed within the enclosed space, and to decide whether the letter would have covered the mark. We manipulated the difficulty of generating the images by varying the complexity of the letters. Kosslyn et al. (1988) found that images of more complex letters are more difficult to generate than simple ones. Within each level of complexity, half of the trials included 'x' marks that would have been covered by the letter, and half included 'x' marks that would not have been covered by it. We examined both the time to respond and the errors subjects made.

We found that both age groups had more difficulty imaging more complex letters in this task, replicating previous results, but this difference was larger for the older people. According to our theory, more complex patterns are imaged by (1) accessing a stored description of the arrangement of parts in associative memory, and then (2) forming images of the parts one at a time. Thus, the effects of age could reflect the process of looking up and using a description to arrange the parts or the process of activating the individual parts. Consistent with our theory, the subjects made more errors and required more time to evaluate probes that fell on segments that would be drawn late in the sequence of strokes than those that fell on segments near the beginning of the drawing sequence. In addition, the rate of increase in errors was much larger for older subjects than for young ones. Thus, we have evidence that the part generation process is affected by age.

The scanning task required the subjects to study a rectangular-ring shape, which resembled a square donut that was composed of black and white squares. After the subject studied the pattern of black and white squares, an arrow appeared within the ring for 50 ms. The arrow appeared in different places within the ring and was presented at eight orientations. Following the brief flash

of the arrow, the display was removed. The subjects' task was to decide whether the arrow pointed to a black or to a white square. All of the rectangular-ring shapes included three black squares, which were located in different places along the perimeter. The arrow was positioned at three distances from the target square, which required the subjects to scan different distances; on half of the trials the arrow pointed to a black square, and in the other half it pointed to a white square.

The response times and errors increased with greater distances to be scanned, replicating previous results (see Kosslyn 1980). However, in contrast to the image generation findings, the increase in response time for greater distances was the same for both age groups, as was the increase in errors. Thus, we not only have evidence that the processes that control the location of the attention window during "image inspection" are distinct from those that generate images, but also that at least some image inspection processes are not affected by age in the same way as the image generation processes.

The image maintenance task was a variant of the generation task; instead of generating visual images from memory, this task required the subjects to retain an image. The subjects studied a pattern presented within a set of four brackets placed at the vertices of an otherwise invisible rectangle. The pattern consisted of one, two, or three perceptual units, formed by juxtaposing black squares to form bars and shapes. After the subject studied the pattern, it was removed; 2500 ms later an 'x' mark was presented within the four brackets, and the subjects were asked to decide whether the shape would cover the 'x' mark. On half of the trials, the shape would have covered the 'x' mark, and on half it would not have.

Both old and young subjects found this task more challenging when more complex stimuli were used, as indicated by increased response times and errors. However, the increase was the same when we compared the one-unit (a bar) and three-unit stimuli. The most interesting finding was for the two-unit stimuli. Young people evaluated them as quickly as one-unit stimuli, whereas old people evaluated them as slowly as the three-unit stimuli. One account for this finding is that young subjects could group two units and encode them as easily as a single bar, whereas old people could not. We assume that this grouping process reflects a "strategy" whereby top-down processes guide attention to group components. Thus, we conjecture that although top-down processes can shift attention as well in old age as in youth, they are less effective at other operations. This is intriguing because shifting attention probably relies on subcortical mechanisms (see Posner and Petersen 1990), whereas the grouping strategy may rely on cortical mechanisms.

Finally, the image rotation task required the subjects to decide whether two shapes were identical, regardless of their orientations. The two shapes were shown simultaneously, and had the same orientation (with no angular disparity) or an angular disparity of 90, 135, or 180 degrees. Half of the stimuli in the pairs presented at each orientation were identical, and half contained mirror-reversed versions of the stimuli. This task is a modified version of the task devised by Shepard and Metzler (1971), who found a linear increase in response time with increases in angular disparity.

Replicating previous results, we found that response times and errors increased with increased angular disparity, which presumably required the subjects to perform more "mental rotation" to align the figures prior to comparing them. In addition, the increase in errors with angular disparity was much more severe for the older subjects. Our finding of increased difficulties in mental rotation with age replicates that of Cerella et al. (1981) and Gaylord and Marsh (1975). Because we examined the slope of the increase, this finding reflects the processes that shift orientation *per se*, and not those involved in encoding the form.

In summary, the results suggest that older people have relative difficulty using top-down processing to access associative memory in the course of generating images, in using top-down processing to organize forms into relatively few perceptual units, and in rotating images. All of these processes appear to involve frontal lobe function. However, the older subjects could shift attention over an image as well as younger subjects, a process which we also speculate involves frontal lobe functions. There is at least one major difference between the role of the frontal lobes in scanning and in the other abilities: the other tasks all involve accessing stored information to guide a sequence of events. To generate an image, one must arrange a series of segments on an image. To maintain the image effectively, one must organize segments and then encode them. To rotate, one must shift an imaged form through a set of distinct increments. It is well known that the frontal lobe has a special role in sequencing events (e.g., Luria 1980), and we suspect that this function is affected by normal aging.

Alzheimer's Disease

Alzheimer's disease is characterized by a wide range of clinical disorders (Schwartz et al. 1990; Semple et al. 1982). Semple et al. (1982) described a number of distinct features of the disease, including memory deficit, spatial disorientation, aphasia, apraxia, and the deterioration of personality. If all of the clinical features of Alzheimer's disease are different manifestations of a single underlying cause, we are left with the puzzle of why such a cause would have such a wide range of effects. Our approach leads us to suggest that the disease can affect some parts of the brain more severely than others (cf. Reisberg 1983). Indeed, there may be different varieties of the disease, with different types affecting different neural structures most severely.

And in fact, Albert and Lafleche (1991) argue that there are two distinct subtypes of Alzheimer's disease; both are characterized by memory deficits, but one also has spatial deficits whereas the other also has language deficits. Presumably, these different deficit profiles arise because different parts of the brain have been affected. Indeed, it is possible that the spatial type of Alzheimer's disease represents a drastic extension of the normal process of cognitive aging. If so, then structures that suffer relatively early during the course of normal aging may be particularly susceptible to the effects of the disease.

Our findings suggest that at least some subcortical structures may be relatively resistant to the effects of aging. Posner and Petersen (1990) argue that the superior colliculus is involved in shifting attention, and we found no deficit in image scanning over normal aging. This finding may suggest that the subcortical structures responsible for scanning are more resistant to the effects of neural deterioration than are certain cortical areas, which may also imply that the abilities these structures support would be relatively intact in the spatial type of Alzheimer's disease. To our knowledge, this possibility has not yet been investigated.

On the other hand, we have hypothesized that certain frontal lobe functions may be impaired over the course of normal aging. If the spatial type of Alzheimer's disease is a severe extension of the normal aging processes, then we would expect similar deficits in these patients. Although Alzheimer's disease is not usually characterized in terms of its effects on frontal lobe function (Martin 1990), Alzheimer's patients often do in fact show signs of frontal lobe damage late in the course of the disease (Schwartz and Chawluk 1990). Indeed, at least part of their difficulties in naming objects may reflect difficulties in the process of accessing information from long-term memory, which may depend on frontal structures (cf. Luria 1980). Moreover, some Alzheimer's disease patients show deficits associated with frontal lobe functions early in the course of the disease (Albert and Lafleche, 1991). These deficits include problems in sequencing, monitoring, and shifting behavior.

In addition, Alzheimer's disease apparently can selectively affect parietal and temporal cortex, which reportedly has distinct effects on spatial orientation and language (Appell et al. 1982; Cummings et al. 1985). It is of interest to discover whether normal aging affects these structures to the same *relative* degree as Alzheimer's disease.

In short, it would be of great interest to compare spatial deficits in normal aging and Alzheimer's disease, using fine-grained tasks that assess distinct aspects of spatial processing. It is possible that the spatial variety of Alzheimer's disease simply amplifies normal trends; alternatively, it may disrupt processing in ways that do not occur in the course of normal aging.

Conclusions

Research on visual mental imagery suggests that a set of component subsystems works in concert to produce various aspects of imagery; different combinations of processes are used to generate, maintain, inspect, and transform images. We have offered hypotheses about which brain structures support each component process, and summarized some initial evidence that normal aging affects some components more than others. It will be of interest to discover whether measures of cortical and subcortical degradation in different varieties of Alzheimer's disease allow us to predict particular profiles of imagery deficits.

In all likelihood, the present theory will be useful for understanding some aspects of these patient's deficits, but fall short in providing a detailed understanding. Thus, trying to use the theory to understand their deficits might

not only illuminate aspects of Alzheimer's disease, but also might enrich the development of the theory more generally.

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