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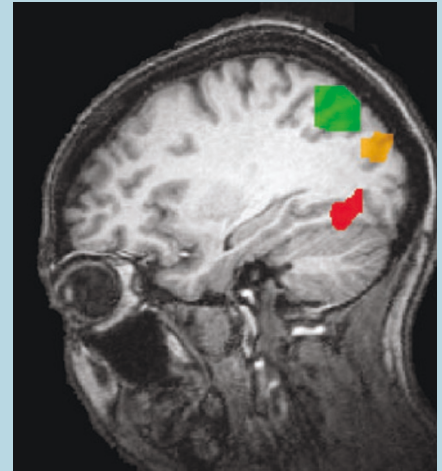
Total recall

The importance of visual short-term memory is clear to anyone who has ever played the children's card game that requires players to identify identical face-down cards at different locations. Visual short-term memory is the temporary buffer that stores visual information. Behavioral studies indicate that this buffer can store up to four objects, but more recent evidence indicates that the maximum number of objects that can be stored becomes smaller as object complexity increases. It is therefore unclear whether visual short-term memory capacity is limited to a fixed number of objects or if it is variable.

In a paper in *Nature* ('Dissociable neural mechanisms supporting visual short-term memory for objects', doi:10.1038/nature04262), Yaoda Xu and Marvin Chun resolve this controversy by using functional magnetic resonance imaging (fMRI) to dissociate object representations in parietal and occipital cortices. Observers were asked to detect a change in a simple or complex shape feature in the same set of objects. The number of objects in a set was varied. Observers did better when they had to detect a change in a simple feature and also when the number of objects was small. The authors found a similar interaction in the superior intraparietal sulcus (green in the picture) and the lateral occipital cortex (red), which tracked behavioral performance, but only for simple shape features, not complex ones. In contrast, activation in the inferior parietal sulcus (orange) tracked overall performance based only on the number of objects seen, regardless of whether observers judged simple or complex shape features. In control experiments, the authors ruled out perceptual processing limitations and spatial location as an explanation for these results, and also correlated the observed activity with the encoding and maintenance phases of visual short-term memory.

These results indicate that there are differing representations for visual short-term memory in the brain. Whereas the inferior parietal sulcus representation is fixed by the number of objects, object representation in the superior parietal sulcus and the lateral occipital cortex varies according to the complexity of the objects being held in visual short-term memory. The inferior parietal sulcus representation is thus likely to be the mechanism determining the maximum number of objects that can be held in visual short-term memory and may determine capacity limitations in tasks such as subitizing and multiple object tracking. The superior parietal sulcus and lateral occipital cortex representation are more likely to contain detailed representations of objects. These results demonstrate that visual short-term memory capacity is determined both by object number and by object complexity.

Charvy Narain



Perceived size matters

Philipp Sterzer & Geraint Rees

Activity in early visual processing areas is often thought to reflect physical input from the retina, rather than conscious perception. A new study now finds that activity in V1 corresponds to perceived rather than actual object size.

Try this quick do-it-yourself experiment: look at an illuminated light bulb for a few seconds and then view the afterimage on

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your hand and finally on a nearby wall. The afterimage seems bigger as the surface on which it is viewed becomes farther away. This illusion¹, reported by Emmert over one hundred years ago, demonstrates one of the most intriguing aspects of vision: even when objects cast exactly the same size pattern of light on the retina, they appear to be markedly different in size when viewed at different distances. In going from retinal image to conscious perception, the visual system is

therefore able to factor in perceived distance to change how big something looks.

Exactly how the visual system achieves this feat remains unclear. It was traditionally assumed that early visual processing areas primarily reflect the physical input from the retina, whereas activity in higher-order areas more closely resembles conscious perception. Such an account would hold that the perceived size of an object would more closely match activity in higher visual

areas. However, in this issue, Murray and colleagues² find a very different pattern of results. They used functional magnetic resonance imaging (MRI) to measure the spatial pattern of activity in human primary visual cortex (V1) while volunteers viewed objects that were physically the same size (and therefore produced identical patterns of retinal input) but were perceived as different in size. Surprisingly, the spatial extent of activity in the very first cortical visual area (V1) reflected not the size of the retinal input, but instead the perceived size of the object. This remarkable finding challenges our notion that V1 contains a very precise one-to-one map of retinal input, and for the first time provides a link between the spatial extent of what we perceive and the exact spatial distribution of activity in human V1.

The authors measured brain activity while subjects viewed pictures of identically sized spheres placed in a picture of a three-dimensional (3D) hallway. A compelling size illusion is immediately apparent (Fig. 1); the sphere at the end of the hallway looks markedly bigger than the one at the start, even though the actual size of the two spheres is exactly the same. Indeed, when subjects were asked to compare the size of these objects with two-dimensional (2D) flat disks (presented on a background without 3D cues), they judged the front sphere to be slightly smaller than the equally sized 2D disk and the back sphere to be larger. The contextual cues to depth in the 3D scene (textural gradients and linear perspective) affect the perceived size of the objects.

Using retinotopic mapping to delineate primary visual cortex, Murray and colleagues examined whether the size of activation patterns in V1 differed when subjects looked at either the front or back spheres. Remarkably, when the sphere that subjects were looking at was perceived to be bigger (due to the contextual cues), activity in V1 spread over a larger area than when it was perceived to be smaller, even though the size of the retinal image produced by the spheres was identical. Activity at the earliest stages of cortical processing does not therefore simply reflect the pattern of light falling on the retina. Somehow the complex three-dimensional cues present in the scene (Fig. 1) can be integrated to take into account perceived depth in the representation present in V1.

As V1 is a relatively large cortical area relative to the spatial resolution of functional MRI, Murray and colleagues were able to compare in detail the size of the activation produced by purely perceptual (illusory) variations in object size and physical changes

in object size. They compared the difference in the distribution of V1 activity between the perceptually 'bigger' and 'smaller' spheres (Fig. 1) with that between two-dimensional disks that physically matched the perceived size difference. They found strikingly similar differences in V1 activity patterns in each case, suggesting that differences in perceived size (rather than retinal input) matter for V1. This further strengthens the claim that the V1 representation of an object closely reflects its perceived size. In other careful control experiments, Murray and colleagues ruled out other possible explanations, such as the local contextual cues altering perceived brightness (which can potentially affect V1 activation³) rather than just perceived size.

Murray and colleagues could not determine precisely where this effect of perceived size on V1 activity arises because they could not examine activity beyond V1 for technical reasons. The visual system must combine information about the perceived depth of an object (provided by the environmental context in Fig. 1) with the projection of that object on the retina. Computing perceived depth from two-dimensional pictorial cues such as linear perspective and texture gradients is associated with activity in parietal cortex^{4,5}. Presumably, such signals reflecting perceived depth can influence V1 through feedback signals that influence the size of the object representation. However, whether the object representation in V1 causes the conscious perception of size remains an open question. Intriguingly, the perceived size of afterimages generated by stimulating the blind hemifield of an individual whose primary visual cortex has been surgically removed nevertheless obeys Emmert's law⁶. This suggests that activity in areas other than V1 may be sufficient to support scaling of perceived size for at least some types of image with perceived distance. A closer characterization of the functional role of V1 in the conscious perception of size therefore remains an intriguing topic for future research.

This work is not the first to show that V1 activity can be strongly linked to conscious perception rather than to physical (retinal) stimulation⁷. It is also clear that neural processing in V1 reflects not just feed-forward signals but also feedback influences from higher areas⁸. However, this work not only provides a particularly clear and compelling example of these properties but also, for the first time, clearly links the spatial extent of what we perceive (rather than, for example, contrast or direction of motion) to the spatial extent of activity in V1. More

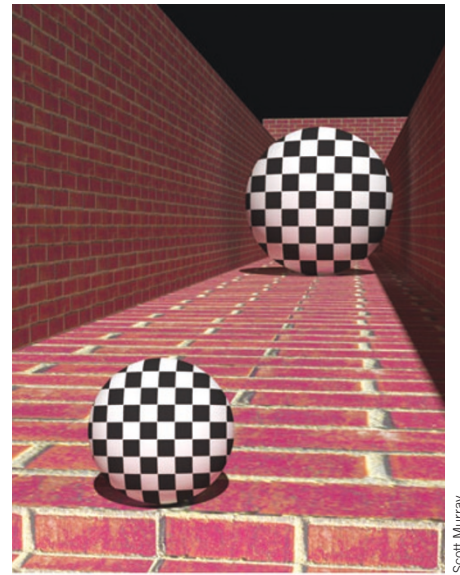


Figure 1 A color picture of the stimuli used in the experiment. The two spheres are actually the same size.

fundamentally, these findings force us to re-evaluate the notion of a 'hard-wired' retinotopy in V1. The finding that V1 contains a topographic map of the retinal projection of the visual field has been central to visual neuroscience^{9,10}. Instead it now seems that the topographic map in V1 can be modified dynamically according to the perceived size of an object. This has important implications not only for understanding the role of V1 in visual processing but also in practical terms. For instance, it has become common practice in functional MRI studies focusing on early visual areas to functionally localize spatially delimited regions of interest using retinotopic mapping. The general usefulness of this approach notwithstanding, future studies will have to take into account the possibility that visual context can dynamically modify this retinotopy, even in early visual areas.

Dynamic shifts in how retinal outputs map onto cortical targets (such as the retinotopic maps in V1) are a key component of an influential computational model¹¹ that seeks to resolve computational problems in the domains of stereopsis (depth perception from binocular cues), spatial attention and motion perception. Thus, flexible mappings between arrays of neurons at different levels of the visual pathway may reflect a common computational strategy for optimal vision. The limits of this 'flexible retinotopy' (ref. 12) will need to be probed and the fine-grained neural mechanisms uncovered through complementary studies

in nonhuman primates. At a single neuron level, primate V1 responses show signals that change according to the distance of an object^{13,14}, forming a potential neural substrate for the dynamic changes observed at a much coarser spatial scale by Murray and colleagues.

Indeed, at a fine-grained level, their findings also raise intriguing questions about whether a V1 representation of the environment that reflects perceived depth and size can be internally coherent. For example, when two objects at different perceived depths partially occlude each other, correct border assignments may be particularly complex as portions of the objects adjacent to the border may be relatively displaced according to perceived depth. The current observation

that the near and far objects were judged to appear both smaller and larger with respect to an equivalently sized two-dimensional object may suggest a 'push-pull' mechanism for maintaining coherence in a spatially distributed V1 representation of the subjects' perceptions.

Taken together, these compelling findings force us once again to consider a revised model of visual processing in which V1, far from being a passive feed-forward recipient of retinal signals, instead flexibly combines retinal and extraretinal signals to potentially build an integrated representation of the perceived visual environment. Future study of how V1 activity relates to human consciousness will doubtless continue to be both interesting and informative.

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Quantifying motor neuron loss in ALS

Amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease) leads to paralysis from the death of motor neurons in the spinal cord and brainstem. It is incurable, and patients typically die within three to five years of disease onset. Neurodegenerative diseases like ALS can progress slowly, with years of clinically undetectable symptoms followed by rapid deterioration. Although ALS selectively targets motor neurons, it has remained unclear whether particular synapses are selectively targeted and whether these synapses are lost gradually or abruptly.

In an article in this issue (page 408), Pico Caroni and colleagues addressed this issue by creating a quantitative map of the innervation of hindlimb muscle compartments by motor neurons in the mouse. They then went on to study the mechanisms of early disease progression in a mouse model of ALS.

Motor neurons innervating skeletal muscle fibers are subdivided into three functional subtypes—fast twitch and fast fatiguable (FF), fast twitch and fatigue resistant (FR) and slow twitch (S). The authors used transgenic mice expressing green fluorescent protein in only a few neurons and mapped the distribution of all synapses made by individual motor neurons in the lateral gastrocnemius muscle. Once they created a topographic map of motor neuron innervation, they analyzed denervation patterns in mice containing a mutation in the enzyme superoxide dismutase (SOD1). In this familial ALS mouse model, they found that FF axons were selectively affected early on in the disease and that these abruptly disconnected from their peripheral synapses when the mice were 48–52 days old. FR motor neurons innervating the same muscle compartments compensated initially for this loss by reinnervating neuromuscular junctions (NMJs) on the muscle fibers, but over time, were less able to maintain the additional NMJs. They then started pruning their nerve branches by the time the mice were 80–90 days old. S-type motor neurons were particularly resistant to disease, and maintained expanded motor units up to the time the mice died.

What makes the FF and FR motor neuron axons selectively vulnerable to disease? The authors did cross-innervation experiments and nerve crush studies and concluded that the early vulnerability of FF motor neurons reflects a vulnerability of the presynaptic motor neuron axon rather than its target muscle or peripheral synapses. They also found that axonal transport was particularly vulnerable in FF and to a lesser degree in FR axons, leading to synaptic vesicle stalling and loss from NMJs. In the figure, the NMJ in the center has lost all synaptic signal (green, synaptic vesicle marker SV2; red, acetylcholine receptor) but is still innervated. Other NMJs may be less affected, like the lower one in the figure. Daily applications of the growth factor ciliary neurotrophic factor (CNTF) protected FF axons from synaptic vesicle loss and peripheral pruning and also helped to maintain the expanded size and innervation of compensating FR motor neuron axons. CNTF helped to boost axonal resistance to disease by causing neurofilament density reductions in both FF and FR neurons and by preventing the upregulation of an anti-apoptotic protein, Bcl2a1-a, in motor neurons.

By providing a quantitative account of the selective vulnerability of different motor neuron populations during the progression of disease, this work opens up new possibilities for treating ALS and related motor neuron disorders.

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