process variance, as population sizes at the onset and termination of the experimental seasons could be determined without sampling error.

Predation rates were estimated by applying a logistic regression model on the population-specific proportion of radio-tracked females depredated by birds. Fecundity was estimated as the product of mean litter delivery rate and mean litter size of all adult females (older than 40 days) in each population.

Transect survey of regional vole abundance variation

We used trapping data from three trapping sites (numbers 19–21)[8] located at the same altitude (250 m) in the neighbouring valley to Glomma, the Rena valley. The habitat and the landscape features were similar to those surrounding the experimental plots at Evenstad. The distances between Evenstad and the transect sites (19–34 km) were shorter than the local synchrony domain (about 40 km) of small rodent populations along the transect[8]. The mean number of microtine rodents (*Clethrionomys glareolus*, *Microtus agrestis* and *M. oeconomus* combined) snap-trapped per station each year was used as a yearly abundance index. Pooling the species is justified because of inter-specific population synchrony[2].

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1. Ranta, E. & Kaitala, V. Travelling waves in vole population dynamics. *Nature* **390,** 456 (1997).
2. Hansson, L. & Henttonen, H. Rodent dynamics as community processes. *Trends Ecol. Evol.* **3,** 195–200 (1988).
3. Bjørnstad, O. N., Ims, R. A. & Lambin, X. Spatial population dynamics: analysing patterns and processes of population synchrony. *Trends Ecol. Evol.* **14,** 427–432 (1999).
4. Ranta, E., Kaitala, V. & Lundberg, V. P. The spatial dimension in population dynamics. *Science* **278,** 1621–1623 (1997).
5. Grenfell, B. T. *et al.* Noise and determinism in synchronized sheep dynamics. *Nature* **394,** 674–677 (1998).
6. Blasius, B., Huppert, A. & Stone, L. Complex dynamics and phase synchronization in spatially extended ecological systems. *Nature* **399,** 354–359 (1999).
7. May, R. M. Crash tests for the real. *Nature* **398,** 371–372 (1999).
8. Steen, H., Ims, R. A. & Sonerud, G. A. Spatial and temporal patterns of small rodent population dynamics at a regional spatial scale. *Ecology* **77,** 2365–2372 (1996).
9. Bjørnstad, O. N., Stenseth, N. C. & Saitoh, T. Synchrony and scaling in dynamics of voles and mice in northern Japan. *Ecology* **80,** 622–637 (1999).
10. Lambin, X. *et al.* Spatial asynchrony and periodic travelling wave in cyclic field vole populations. *Proc. R. Soc. Lond. B* **265,** 1491–1496 (1998).
11. Korpimäki, E. & Krebs, C. J. Predation and population cycles of small mammals. A reassessment of the predation hypothesis. *BioScience* **46,** 754–764 (1996)
12. Aars, J., Johannesen, E. & Ims, R. A. Demographic consequences of movements in subdivided root vole populations. *Oikos* **85,** 204–216 (1999).
13. Steen, H. Low survival of long distance dispersers of the root vole (*Microtus oeconomus*). *Ann. Zool. Fennici* **31,** 271–274 (1994).
14. Ims, R. A. & Andreassen, H. Effects of experimental habitat fragmentation and connectivity on root vole demography. *J. Anim. Ecol.* **68,** 839–852 (1999).
15. Andreassen, H. P. & Ims, R. A. The effect of experimental habitat destruction and patch isolation on space use and fitness parameters in female root vole *Microtus oeconomus*. *J. Anim. Ecol.* **67,** 941–952 (1998).
16. Clobert, J. *et al.* (eds) *Causes and Consequences of Dispersal at the Individual, Population and Community Level* (Oxford Univ. Press, in the press).
17. Wolff, J. O. Population regulation in mammals: an evolutionary perspective. *J. Anim. Ecol.* **66,** 1–13 (1997).
18. Ims, R. A. & Steen, H. Geographic synchrony in microtine population cycles: a theoretical evaluation of the role of nomadic avian predators. *Oikos* **57,** 381–387 (1990).
19. Krebs, C. J. Population cycles visited. *J. Mamm.* **77,** 8–24 (1996).
20. Stenseth, N. C. & Ims, R. A. *The Biology of Lemmings* (Academic, London, 1993).
21. Hanski, I. *et al.* Population oscillation of boreal rodents: regulation by mustelid predators leads to chaos. *Nature* **364,** 232–235 (1993).
22. Turchin, P. & Hanski, I. An empirically based model for latitudinal gradients in vole population dynamics. *Am. Nat.* **149,** 842–874 (1997).
23. Heikkilä, J., Below, A. & Hanski, I. Synchronous dynamics of microtine rodent populations on islands in Lake Inari in northern fennoscandia: evidence for regulation by mustelid predators. *Oikos* **70,** 245–252 (1994).
24. Korpimäki, E. & Norrdahl, K. Experimental reduction of predators reverses the crash phase sphase of small-rodent cycles. *Ecology* **79,** 2448–2455 (1998).
25. Viitala, J. *et al.* Attraction of kestrels to vole scent marks visible in ultraviolet-light. *Nature* **373,** 425–427 (1995).
26. Steen, H. Untangling the causes of dissappearance from a local population of root vole, *Microtus oeconomus*: a test of the regional synchrony hypothesis. *Oikos* **73,** 65–72 (1995).
27. Reid, D. G., Krebs, C. J. & Kenney, A. Limitation of collared lemming population-growth at low densities by predation mortalilty. *Oikos* **73,** 387–398 (1995).
28. Norrdahl, K. & Korpimäki, E. Mortality factors in a cyclic vole populations. *Proc. R. Soc. Lond. B* **261,** 49–53 (1995).
29. Johannesen, E., Andreassen, H. P. & Steen, H. C-J-S modelling revealed no effect of radio collars on survival of root voles. *J. Mamm.* **78,** 638–642 (1996).

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Tracking an object through feature space

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Visual attention allows an observer to select certain visual information for specialized processing. Selection is readily apparent in 'tracking' tasks where even with the eyes fixed, observers can track a target as it moves among identical distractor items[1]. In such a case, a target is distinguished by its spatial trajectory. Here we show that one can keep track of a stationary item solely on the basis of its changing appearance—specified by its trajectory along colour, orientation, and spatial frequency dimensions—even when a distractor shares the same spatial location. This ability to track through feature space bears directly on competing theories of attention, that is, on whether attention can select locations in space[2–4], features such as colour or shape[5–7], or particular visual objects composed of constellations of visual features. Our results affirm, consistent with a growing body of psychophysical[8–13] and neurophysiological[14–16] evidence, that attention can indeed select specific visual objects. Furthermore, feature-space tracking extends the definition of visual object[17] to include not only items with well defined spatio-temporal trajectories[18], but also those with well defined featuro-temporal trajectories.

In this investigation, observers tracked and made judgements about a circular striped 'Gabor' patch that dynamically changed its orientation, spatial frequency and colour, but never its spatial location. Along these feature dimensions the Gabor smoothly changed: spinning, say, clockwise for a while then counter-clockwise; changing gradually back and forth between a few broad stripes and many thin stripes; and altering its saturation, ranging smoothly between a patch made up of grey and black stripes to a patch made up of red and black stripes, through all the intervening saturation levels of red.

Our aim was to test whether observers can track such an item through feature space, but we were also interested in determining which of location-, feature-, or object-based theories of visual attention could best account for this ability, if it existed. Location and 'objecthood' can be difficult to distinguish, as typically a single object occupies a single location[19,20]. We separated location from objecthood in our experiments by completely superimposing two such Gabor patches (Fig. 1a) such that there was no spatial distinction to support selection by location-based attention: individual parts of each Gabor changed dynamically, and were at the limits of the resolution of location-based attention[4,21,22] (the spatial frequency of the 1-degree-diameter Gabor ranged dynamically between 1.5 to 8 cycles per degree; thus the width of a single stripe ranged from 20 to 4 arcmin). The Gabors appeared to observers as simultaneously present and transparently layered on one another, although there was no noticeable separation in depth (Fig. 1b).

In experiment 1, observers were instructed to track one of the two superimposed Gabors. During the tracking interval, the Gabors frequently 'passed' each other along one or more dimensions (Fig. 1c). (This ensured that feature-based attention could not simply pick out the target on the basis of some constant featural difference. Unless this is done, results that are consistent with object-based attention are subject to criticisms owing to the possible contributions of feature-based attention. For instance, this is of concern in studies where two stimuli always have, say, different motion directions throughout the entire trial[7]. Although location-based attention may be foiled by the superimposition, feature-based attention may still pick out one of the stimuli by selectively enhancing its direction of motion.) The four observers (naive: JT, DA, DK; expert: EB) successfully picked the target Gabor with 90% accuracy.

How were observers able to accomplish this tracking through feature-space? Observers reported that the two superimposed Gabors perceptually segregated from one another (although occasionally they appeared as a single entity, typically when the two objects had a near-miss or actually 'collided' in feature space). The segregation of superimposed stimuli has been observed in studies of motion transparency[5,23]. In addition, judging from informal observations of our stimuli, the simultaneous changes along the orientation, colour and spatial frequency dimensions result in more compelling transparency than that which results from changes along any one, or pair, of these dimensions alone. Observers also reported that attending to a particular Gabor resulted in an increase of its salience, in a manner not unlike figure–ground segmentation. The attended Gabor became the figure and the distractor Gabor receded into the ground[24,25]. As our stimuli were constructed to eliminate contributions from location- and feature-based attention, the ability to track through feature space alone is suggestive evidence for object-based attention.

Although they are not mutually exclusive, location-, feature- and object-based theories deal with our compound Gabor stimulus quite differently. Feature-based theories treat the stimulus as a mix of colour, orientation and spatial frequency information, any of which may be selectively enhanced by attention; location-based theories treat the stimulus as a unitary stream of information, the whole of which may be enhanced[26]; but only object-based attention theories can treat the stimulus as two unitary streams of information, each corresponding to one of the superimposed Gabors, and each a legitimate target for visual attention. Moreover, object-based theories predict that when observers attempt to attend to a particular feature of one of the Gabors in our stimulus they actually, by default, attend to the object as a whole; consequently, processing is enhanced for all of its features[10]. This leads to two predictions that can be tested psychophysically. First, in contrast to location-based theories, object-based theories predict that selective enhancement of an object can take place even if there is another object that is spatially superimposed. Second, in contrast to feature-based theories, selective attention to any feature of an object should also enhance processing of its other features.

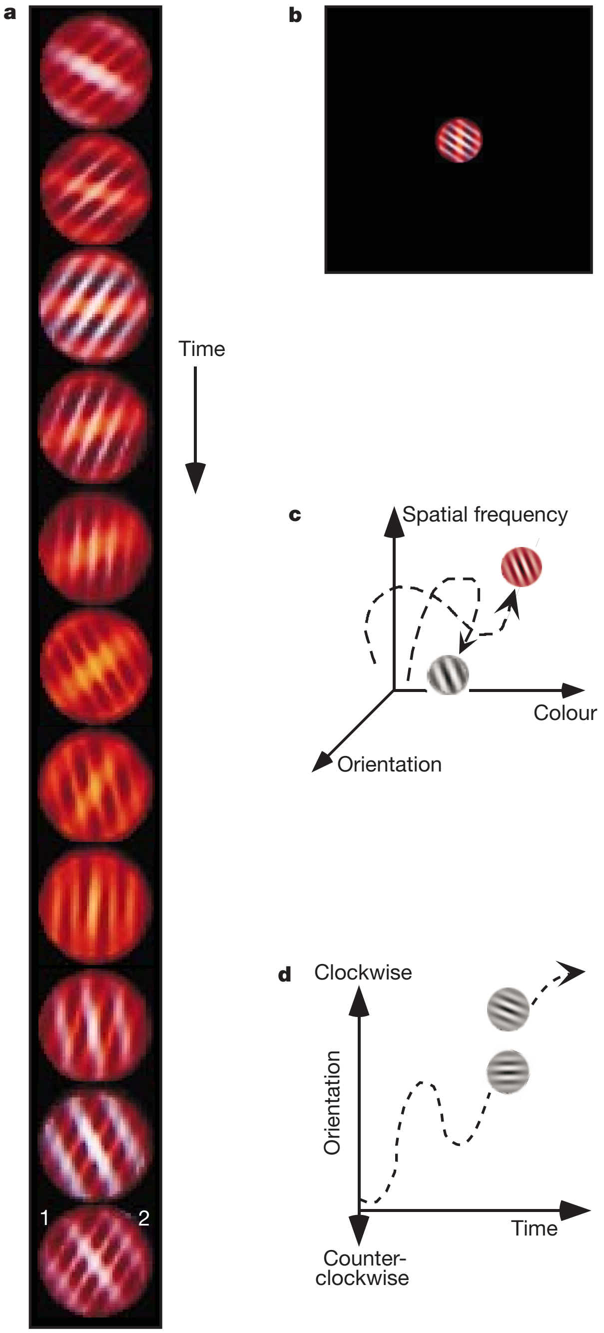

Figure 1 Objects in feature space. **a**, Snapshots taken every 250 ms of two superimposed Gabor patches drifting in a feature space defined by the dimensions of colour, orientation and spatial frequency. In experiment 1, observers tracked one target Gabor for 10 seconds, then picked out the target by reporting one of two small number labels (shown here in the last snapshot). **b**, Schematic of display, illustrating that the two Gabors were always stationary in space, and superimposed, at fixation. **c**, Diagram of the two Gabors drifting in feature-space. **d**, Diagram of a clockwise 'jump'. Gabors also jumped along the colour and frequency dimensions.

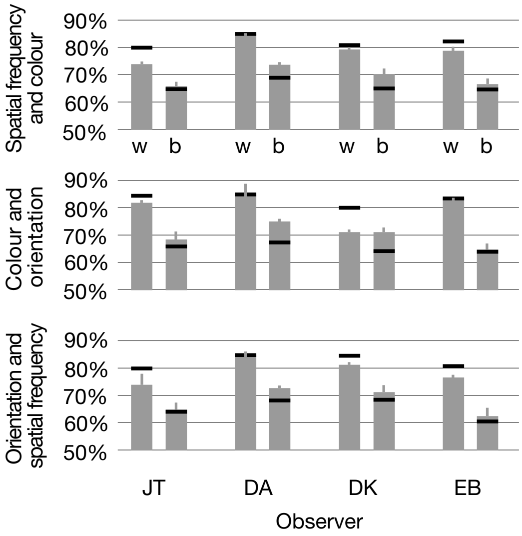

Figure 2 Experiment 2 results; percentage correct jump-direction judgements for each condition and observer. Conditions are labelled on the left, and specify the pair of feature dimensions observers were instructed to attend to, and make judgements about, for that particular block of trials. Pairs of bars show performance in within-object (w) and between-object (b) conditions, respectively. Spikes on the bars indicate standard errors. The black line above each within-object bar is the average performance from single-task control conditions, which is the theoretical maximum achievable performance. The black line on each between-object bar is the theoretical minimum performance. Data is shown for three naive (JT, DA, DK) observers and one expert observer (EB).

In experiment 2, we tested these predictions by instructing observers to perform two concurrent tasks. Performance in concurrent tasks reveals how the tasks compete for processing resources. When two tasks do not compete for resources, performance on one should not suffer when the other is performed concurrently (like walking and chewing gum). When two tasks do compete, performance on one of the tasks will suffer when the other task is performed concurrently (like juggling and sign language). Because competition occurs when an attention mechanism is forced to divide its resources, it is possible to determine which type of attention is mediating performance by observing when performance losses occur[27,28].

We introduced a small discontinuity, or "jump", into the trajectory of each target along each dimension and then compared conditions for which a pair of jump-direction judgements was made within a common Gabor (for example, reporting the direction of the colour and orientation jumps for a specified Gabor), with conditions where the same two judgements were divided between the two Gabors (for example, reporting the direction of the colour jump for one Gabor, and the orientation jump for the other). If object-based attention mediates performance in this task, then processing will be enhanced for all of the features of one of the Gabors, but not the features of the other Gabor. Therefore, there should be little or no competition for resources provided that the concurrent judgements are made with respect to a common Gabor. However, if concurrent judgements are divided between the two Gabors, significant competition should result, as in that case attentional resources must somehow be divided between the objects.

This is exactly the pattern of results we found. When observers were asked to make two judgements about the same Gabor, performance was on average 80% correct, very close to the theoretical maximum performance of 83% correct given by single-task control conditions (when observers only had to make one judgement at a time). In other words, observers could make both of these judgements simultaneously almost as well as they made each of them alone (like walking and chewing gum). In contrast, when observers attempted to divide their attention to make the judgements between the two Gabors, performance dropped to 69% correct, quite close to the theoretical minimum of 66% correct that would be achieved if observers could not do both tasks at the same time at all (like juggling and sign language) and instead, for instance, did one task on the even trials and the other on the odd trials (Fig. 2). This asymmetry in the results cannot be accounted for by either location- or feature-based theories.

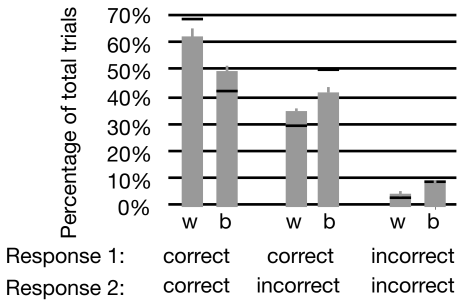

Figure 3 Assessment of 'sharing' versus 'switching' models of attention resources. Observers made two responses in both within-object (w) and between-object (b) conditions; thus, trials fall into three categories (correct/correct, correct/incorrect, or incorrect/incorrect). Bars correspond to the actual percentage of trials in each category, averaged over observer. Spikes on the bars indicate standard errors. Black lines on the within-object bars are the predictions of a pure sharing model, where it is assumed that observers perform both tasks at levels given by single-task control conditions. Black lines on the between-object bars are the predictions of a pure switching model, where observers perform one task at single-task levels, but perform the other at chance.

Observers are thus capable of tracking a single object in spite of a spatially superimposed distractor. But are observers able to track multiple objects simultaneously? In the between-object conditions of experiment 2, observers had both an instruction and a task that encouraged them to attend and track two objects simultaneously. It is clear that observers did much worse in these conditions than in the within-object conditions, where they had only to attend and track a single object. Nevertheless, perhaps observers were actually able to attend to and track both objects at the same time to some extent, that is, to 'share' attentional resources between the two. On the other hand, perhaps observers were unable to share and instead 'switched' attention—sometimes attending to one object, and sometimes attending to the other.

Though both sharing and switching models can account for overall performance, they make very different predictions for the underlying pattern of responses[27]. Specifically, if observers were sharing, then the correctness of responses on the two judgements should show statistical independence. That is, whether or not observers were correct on the jump-direction judgement with respect to one object should not significantly influence their correctness with respect to the other. Alternatively, if observers were switching, then if observers were correct on one judgement, they should be less likely to be correct on the other, and vice versa. A χ^2 test of the between-object data rejected the null hypothesis of statistical independence ($P < 0.005$ for each observer), and therefore of pure sharing of attention. (As predicted by object-based theories of attention, this test performed on the within-object data cannot reject the hypothesis of statistical independence—indicating that observers share resources within an object, that is, simultaneously attend to all its features.) We then used the data from the single-task control conditions in conjunction with pure sharing and pure switching models to predict the proportion of trials in which observers should get both responses correct, both incorrect, and one correct and one incorrect. These predicted values were compared to the frequencies in the actual data (Fig. 3). The pattern is clear: observers approach pure sharing when attending to a single object (because resources were, by default, shared among all the object's features), but approach pure switching when attempting to attend to two objects (because attention could only be devoted to a single object at a time). The result of this analysis, taken together with observers' reports of an inability to attend to both objects simultaneously, indicates that object-based attention limits tracking through feature space at a given location to a single object.

The ability to track through feature-space and our finding of competition for attentional resources between, but not within, superimposed items, implies the operation of object-based attention, but also shows that distinct 'visual objects'[29] need not have distinct spatiotemporal trajectories. Rather, distinct *featuro*-temporal trajectories are sufficient for objecthood and attentional tracking. □

Methods

Stimuli

The basic stimulus was a circular striped 'Gabor' patch (windowed cosinusoid) that dynamically changed its orientation, spatial frequency and colour, but never its location on the screen. This can be conceptualized as a single item that smoothly drifted in a feature-space defined by orientation, spatial frequency and colour dimensions. The trajectory of the Gabor along each of the feature dimensions was random and independent, frequently changing direction and speed along any given dimension. The Gabor did, however, drift with some 'inertia' that made it more likely to continue drifting, along a particular dimension, in the direction it was going (the inertia factor simply places a probability on whether or not the object will change its speed and/or direction along a particular dimension at a given time). In all experiments and conditions, two such Gabors were completely spatially superimposed (Fig. 1a). The Gabors were superimposed by temporally interleaving their images at a rate of 117 Hz (58.5 Hz per item, with one Gabor shown in the even video frames and the other in the odd frames). Observers were seated 100 cm from the 1.76-cm stimulus, which subtended 1 degree of visual angle. The stimulus was presented on an otherwise dark screen. Observers were instructed to maintain fixation on the stimulus during presentation (Fig. 1b). As the trajectories of the Gabors were independent, they frequently 'passed' each other along one or more dimensions (Fig. 1c).

Tracking in feature-space

In experiment 1, observers were presented with the compound stimulus for an initial 1-second fixation interval, giving them an opportunity to attend to the target Gabor, which was identified by being initially oriented 45 degrees clockwise. Both Gabors then began changing along all three feature dimensions for a 10-second tracking interval. At the end of the tracking interval, the Gabors stopped changing, but remained on the screen. Two small number labels appeared above the stimulus (Fig. 1a). One of the labels was aligned with the orientation of one of the Gabors (for instance, if the Gabor ended up tilted, say, a bit clockwise, its label would appear at ‘1 o'clock’), whereas the other label was aligned with the other Gabor. Observers used a keypress to report the label that they thought corresponded to the target item. Observers received positive feedback and a point score to encourage best performance.

Object-based attention

As in experiment 1, in experiment 2, observers viewed the static compound stimulus for an initial 1-second fixation interval. Then both Gabors began changing along all three possible feature dimensions for a 5-s tracking interval. At some random time in the tracking interval, both Gabors exhibited a slight discontinuity in their featural trajectories simultaneously along all three dimensions (colour, spatial frequency and orientation); that is, there was a slight ‘jump’ in the trajectory of each Gabor (Fig. 1d). The directions of the jumps were chosen randomly and independently for each Gabor and dimension, and the sizes of the jumps were fixed at values corresponding to 75% correct jump-direction thresholds determined from baseline psychometric functions of jump-size for each dimension and observer. In any given block of trials, observers were instructed to attend concurrently to a pair of dimensions. After the tracking interval, both Gabors stopped changing, but remained on the screen. Observers then made a keypress to report the direction of the jump (that is, clockwise or counter-clockwise, more or less red, higher or lower spatial frequency) for the pair of dimensions. Single-task control conditions were also run, where observers only needed to attend to, and make jump-direction judgements about, one feature dimension. Observers received positive feedback and a point score.

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1. Pylyshyn, Z. W. & Storm, R. W. Tracking multiple independent targets: Evidence for a parallel tracking mechanism. *Spatial Vision* **3,** 179–197 (1988).
2. Posner, M. I. Orienting of attention. *Q. J. Exp. Psychol.* **32,** 3–25 (1980).
3. Sagi, D. & Julesz, B. Enhanced detection in the aperture of focal attention during simple discrimination tasks. *Nature* **321,** 693–695 (1986).
4. Eriksen, C. W. & Hoffman, J. E. Temporal and spatial characteristics of selective encoding from visual displays. *Percept. Psychophys.* **12,** 201–204 (1972).
5. Cavanagh, P. Attention-based motion perception. *Science* **257,** 1563–1565 (1992).
6. Wolfe, J. M., Cave, K. R. & Franzel, S. L. Guided search: an alternative to the feature integration model for visual search. *J. Exp. Psychol. Hum. Percept. Perform.* **15,** 419–433 (1989).
7. Corbetta, M., Miezin, F. M., Dobmeyer, S., Shulman, G. L. & Petersen, S. E. Attentional modulation of neural processing of shape, color, and velocity in humans. *Science* **248,** 1556–1559 (1990).
8. Duncan, J. Selective attention and the organization of visual information. *J. Exp. Psychol. Gen.* **113,** 501–517 (1984).
9. Valdes-Sosa, M., Cobo, A. & Pinilla, T. Transparent motion and object-based attention. *Cognition* **66,** B13–B23 (1998).
10. Luck, S. J. & Vogel, E. K. The capacity of visual working memory for features and conjunctions. *Nature* **390,** 279–281 (1997).
11. Kahneman, D., Treisman, A. & Gibbs, B. J. The reviewing of object files: object-specific integration of information. *Cogn. Psychol.* **24,** 175–219 (1992).
12. Baylis, G. C. & Driver, J. Visual attention and objects: evidence for hierarchical coding of location. *J. Exp. Psychol. Hum. Percept. Perform.* **19,** 451–470 (1993).
13. Treisman, A. Feature binding, attention and object perception. *Philos. Trans. R. Soc. Lond. B* **353,** 1295–1306 (1998).
14. Driver, J., Baylis, G. C. & Rafal, R. D. Preserved figure–ground segregation and symmetry perception in visual neglect. *Nature* **360,** 73–75 (1992).
15. Valdes-Sosa, M., Bobes, M. A., Rodriguez, V. & Pinilla, T. Switching attention without shifting the spotlight object-based attentional modulation of brain potentials. *J. Cogn. Neurosci.* **10,** 137–151 (1998).
16. O'Craven, K. M., Downing, P. E. & Kanwisher, N. fMRI evidence for objects as the units of attentional selection. *Nature* **401,** 584–587 (1999).
17. Treisman, A. & Paterson, R. Emergent features, attention, and object perception. *J. Exp. Psychol. Hum. Percept. Perform.* **10,** 12–31 (1984).
18. von Hofsten, C. & Spelke, E. S. Object perception and object-directed reaching in infancy. *J. Exp. Psychol. Gen.* **114,** 198–212 (1985).
19. Lappin, J. S. Attention in the identification of stimuli in complex visual displays. *J. Exp. Psychol.* **75,** 321–328 (1967).
20. Bonnel, A. M. & Prinzmetal, W. Dividing attention between the color and the shape of objects. *Percept. Psychophys.* **60,** 113–124 (1998).
21. He, S., Cavanagh, P. & Intriligator, J. Attentional resolution and the locus of visual awareness. *Nature* **383,** 334–337 (1996).
22. Blaser, E., Sperling, G. & Lu, Z. L. Measuring the amplification of attention. *Proc. Natl Acad. Sci. USA* **96,** 11681–11686 (1999).
23. Qian, N., Andersen, R. A. & Adelson, E. H. Transparent motion perception as detection of unbalanced motion signals. I. Psychophysics. *J. Neurosci.* **14,** 7357–7366 (1994).
24. Neisser, U. & Becklen, R. Selective looking: Attending to visually specified events. *Cogn. Psychol.* **7,** 480–494 (1975).
25. Rock, I. & Gutman, D. The effect of inattention on form perception. *J. Exp. Psychol. Hum. Percept. Perform.* **7,** 275–285 (1981).
26. Shih, S. I. & Sperling, G. Is there feature-based attentional selection in visual search? *J. Exp. Psychol. Hum. Percept. Perform.* **22,** 758–779 (1996).
27. Sperling, G. & Melchner, M. J. The attention operating characteristic: examples from visual search. *Science* **202,** 315–318 (1978).
28. Lee, D. K., Koch, C. & Braun, J. Attentional capacity is undifferentiated: concurrent discrimination of form, color, and motion. *Percept. Psychophys.* **61,** 1241–1255 (1999).
29. Scholl, B. J. & Pylyshyn, Z. W. Tracking multiple items through occlusion: clues to visual objecthood. *Cognit. Psychol.* **38,** 259–290 (1999).

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Distinct functions of the two isoforms of dopamine D2 receptors

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Signalling through dopamine D2 receptors governs physiological functions related to locomotion, hormone production and drug abuse[1–7]. D2 receptors are also known targets of antipsychotic drugs that are used to treat neuropsychiatric disorders such as schizophrenia[8]. By a mechanism of alternative splicing, the D2 receptor gene encodes two molecularly distinct isoforms[9], D2S and D2L, previously thought to have the same function. Here we show that these receptors have distinct functions *in vivo*; D2L acts mainly at postsynaptic sites and D2S serves presynaptic autoreceptor functions. The cataleptic effects of the widely used antipsychotic haloperidol[1] are absent in D2L-deficient mice. This suggests that D2L is targeted by haloperidol, with implications for treatment of neuropsychiatric disorders. The absence of D2L reveals that D2S inhibits D1 receptor-mediated functions, uncovering a circuit of signalling interference between dopamine receptors.

Dysfunctions of the dopaminergic system are involved in neurological disorders such as Parkinson's disease, Tourette's syndrome, schizophrenia and in pituitary tumours[1]. Dopamine acts through membrane receptors of the seven transmembrane domain G-protein coupled family. Two classes of dopamine receptor have been defined: D1-like (D1R and D5R) and D2-like (D2R, D3R and D4R) which, respectively, stimulate and inhibit adenylyl cyclase, thereby regulating intracellular cAMP levels[1].

D2 receptors are highly expressed in the striatal complex and pituitary gland. Ablation of this receptor results in locomotor impairment[2–4], altered response to drug abuse[5], pituitary tumours[6,7] and the modification of the electrophysiological characteristics of D2R-expressing neurons[10,11]. Thus, D2Rs have an essential position at the postsynaptic level, and, by acting as autoreceptors[10,12], in the regulation of the dopaminergic system by modulating dopamine release.

D2R has two isoforms, D2L and D2S, which are generated by alternative splicing[9] and co-expressed in a ratio favouring the long isoform, D2L (Fig. 1c, wild type). D2L differs from D2S by the presence of an additional 29 amino acids within the third intracellular loop. This region is implicated in the receptor interaction