

Preattentive Filling-in of Visual Surfaces in Parietal Extinction

Jason B. Mattingley,* Greg Davis, Jon Driver

Unilateral brain damage frequently produces "extinction," in which patients can detect brief single visual stimuli on either side but are unaware of a contralesional stimulus if presented concurrently with an ipsilesional stimulus. Explanations for extinction have invoked deficits in initial processes that operate before the focusing of visual attention or in later attentive stages of vision. Preattentive vision was preserved in a parietally damaged patient, whose extinction was less severe when bilateral stimuli formed a common surface, even if this required visual filling-in to yield illusory Kanizsa figures or completion of partially occluded figures. These results show that parietal extinction arises only after substantial processing has generated visual surfaces, supporting recent claims that visual attention is surface-based.

A key feature of vision is that stimulus events receive substantial processing before being selectively attended. Theories of normal vision have suggested that properties such as color, shape, and motion are coded before being selectively attended (that is, "preattentively") and that selective attention operates subsequently on the results of such low-level processing (1). A crucial test of such processing dichotomies can be provided by studying the selective breakdown of initial preattentive processes and later attentive stages of vision in patients with discrete brain lesions (2). Here we focus on the neuropsychological phenomenon of extinction, which is observed after various brain lesions but especially those involving the right parietal lobe (3).

Although extinction has sometimes been thought to reflect weakened afferent inputs on the contralesional side (4), several observations suggest that in parietal cases it is primarily a disorder of selective attention, in which simultaneous stimuli on the ipsilesional side have a competitive advantage (5). First, parietal extinction patients show preserved detection of single contralesional events, which indicates that afferent pathways on the affected side are relatively intact. Second, parietal extinction occurs even when bilateral stimuli are presented entirely within the ipsilesional (intact) hemifield (6). Third, parietal patients may detect more contralesional targets when told to ignore any concurrent ipsilesional events (6, 7), which suggests that their disorder only arises when two events must compete for attention. A strong prediction arising from this atten-

tional account of extinction is that preattentive visual processes should proceed normally on the contralesional side, with an ipsilesional bias arising only at some later attentive stage.

To test this prediction, we used two types of stimuli that induce visual filling-in for normal people. The first type of stimulus induces filling-in of the kind exemplified in Kanizsa subjective figures (8); these figures arise when edges and brightness are illusorily perceived between inducing elements in the absence of physical luminance discontinuities. The process leading to the perception of such subjective figures is known as "modal" completion (9). The second kind of stimulus induces completion for the visible fragments of an object that seems partly occluded by an intervening surface, a process known as "amodal" completion (9). Both types of completion are of

particular interest because they provide examples of the visual system going beyond the immediate retinal image, toward an interpretation of the probable three-dimensional (3D) sources in the external world (8–10).

Recent evidence has suggested that such visual filling-in may occur preattentively in normal humans (10). If so, and if parietal extinction is indeed a deficit of attentive vision only, then this visual completion should still arise in parietal extinction patients. The present study tests this neuropsychological prediction. In contrast to previous studies of "implicit" processing of extinguished or unreported visual stimuli (11), our experiments identify conditions under which extinguished information can suddenly enter awareness, after visual filling-in between ipsilesional and contralesional events.

Patient V.R. has left-sided extinction after predominantly right-hemisphere damage (Fig. 1). After obtaining informed consent, we tested the hypothesis that parietal extinction is an attentional deficit (5), plus recent claims that attentive vision operates on surface-based representations after completion has arisen (12), by examining whether V.R.'s extinction would be reduced when two simultaneous visual events formed a single coherent surface due to perceptual filling-in (13). Specifically, we arranged two bilateral stimuli so that they could induce the percept of a single Kanizsa subjective surface between them.

In experiment 1, V.R. had to detect the removal of segments from four circular inducers presented in brief visual displays (Fig. 2, A through D). In separate trials,

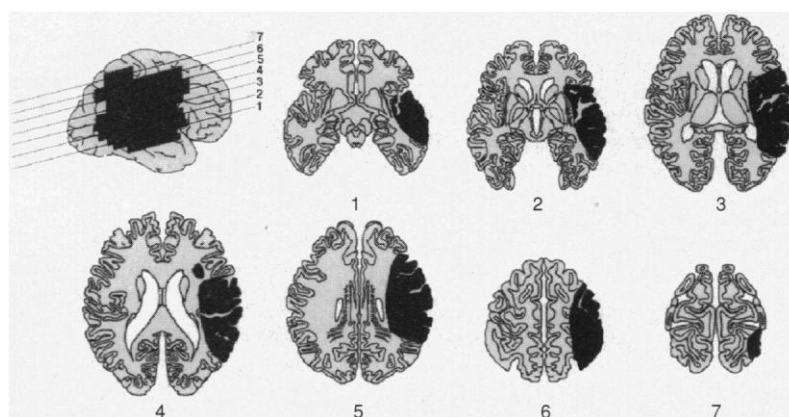


Fig. 1. Reconstruction of cranial computerized tomographic scans from patient V.R., a 66-year-old woman who suffered a stroke in the territory of the right middle cerebral artery. At the top left is shown a lateral view of the right hemisphere with the lesioned area indicated in black. The oblique lines through the lateral view correspond to the numbered transverse sections. These sections show a right lesion involving the inferior, middle, and superior temporal gyri, the supramarginal and angular gyri, the superior parietal lobe, and the sensorimotor and premotor cortex. The lesion extends into the frontal and parietal operculae and the insula and the optic radiations but spares the internal capsule and basal ganglia. A small circumscribed area of infarction (not shown) was also present in the left medial occipital lobe, posterior to the splenium of the corpus callosum [see (17)].

J. B. Mattingley, Department of Experimental Psychology, University of Cambridge, Downing Street, Cambridge CB2 3EB, UK.

G. Davis and J. Driver, Department of Psychology, Birkbeck College, University of London, Malet Street, London WC1E 7HX, UK.

*To whom correspondence should be addressed.

segments could be removed bilaterally, unilaterally, or (in catch trials) not at all (Fig. 2, E and F). After each trial, V.R. indicated verbally the side or sides from which any segments were removed. For "inner" displays (see Fig. 2E), bilateral removal of segments yielded a Kanizsa rectangle between the inducing "Pac-men" (as in Fig. 3A). For "outer" displays (see Fig. 2F), any removed segments faced outward, so that no subjective surface was formed (Fig. 3B). V.R. showed substantial extinction for bilateral outer displays but none for inner displays (see graph in Fig. 3C), which implies that extinction is ameliorated when simultaneous events on the two sides lead

to filling-in processes that form a single new surface.

It remained possible, if unlikely, that V.R.'s improved detection of contralesional stimuli on bilateral inner displays was due merely to the inner-facing Pac-men on the ipsilesional side, rather than to filling-in between the two sides. Accordingly, in experiment 2, the ipsilesional events were now always of the inner type, whereas the contralesional left events were either inner (Fig. 3D) or outer (Fig. 3E); a Kanizsa rectangle was formed on bilateral trials only with left-inner displays (Fig. 3D). V.R. continued to show severe extinction when there was no Kanizsa rectangle (left-outer displays) but again showed relatively little extinction when a Kanizsa rectangle was formed (with left-inner displays; see graph in Fig. 3F). V.R.'s improved detection of contralesional events in bilateral displays evidently arises only when the region between the inducing Pac-men can be filled in from both the ipsilesional and contralesional sides to form a single new surface.

A further factor to consider is that the removed segments were more eccentric in

the outer than in the inner displays (compare A and D with B and E in Fig. 3). To control for this, in experiment 3 we held the eccentricity of removed segments constant, with the control condition now created by leaving a narrow arc across the Pac-men inducers (Fig. 3H). Previous studies in normal people (10) have found that such arc displays do not induce a subjective figure preattentively, despite their close physical similarity to the experimental displays on which they are based (compare G and H in Fig. 3).

V.R. again detected more left segments under bilateral stimulation when a Kanizsa rectangle was induced than she did for comparable arc displays with no subjective surface (see graph in Fig. 3I). These findings replicate those of experiments 1 and 2, while ruling out accounts in terms of target eccentricity. Explanations in terms of weakened afferent inputs from image features (4) are also ruled out, because any such sensory loss should apply equivalently for the arc and Pac-men inducers (Fig. 3, H versus G). We suggest instead that V.R.'s deficit is attentional, with the competitive advan-

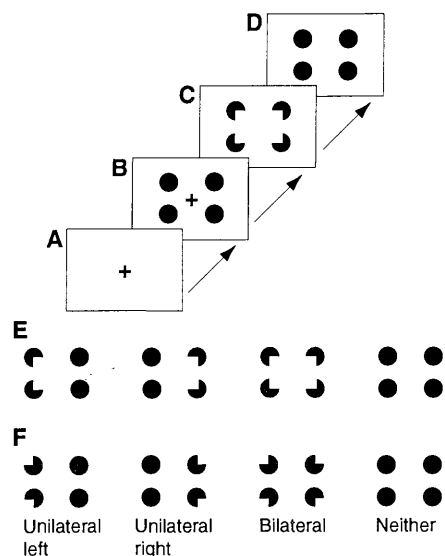


Fig. 2. Example sequence of events (18) for experiments 1 through 3. (A) Each trial began with V.R. fixating a central cross, as verified by an observer positioned behind the display. (B) After 1 s (500 ms in experiment 2), four circles appeared, arranged in a rectangle around fixation. (C) After a further 2 s (1 s in experiment 2), quarter-segments were removed briefly from the circles on the left, right, or both sides or on neither side (to provide catch trials as a control for any guessing). The example in (C) shows a bilateral inner trial, in which segments were removed from both sides to yield a Kanizsa rectangle between them for a short time (19). (D) The segments were then replaced, and full circles remained visible until V.R. responded verbally (saying left, right, both, or none). Experiment 4 had the same sequence of events, except that quarter-segments were removed from all circles on the third frame of every trial. V.R.'s task in experiment 4 was to detect the onset of small dots (1.3° diameter) in the third frame of the display sequence. The dots, which appeared closer to fixation than the Pac-men inducers, appeared on either the left or right, on both sides, or on neither side of fixation. The duration of this third frame was 150 ms, and any dots disappeared as quarter-segments were replaced in the fourth frame (20). (E) Segments to be detected in the four trial types for inner displays (experiments 1 through 3), and (F) for outer displays (experiment 1).

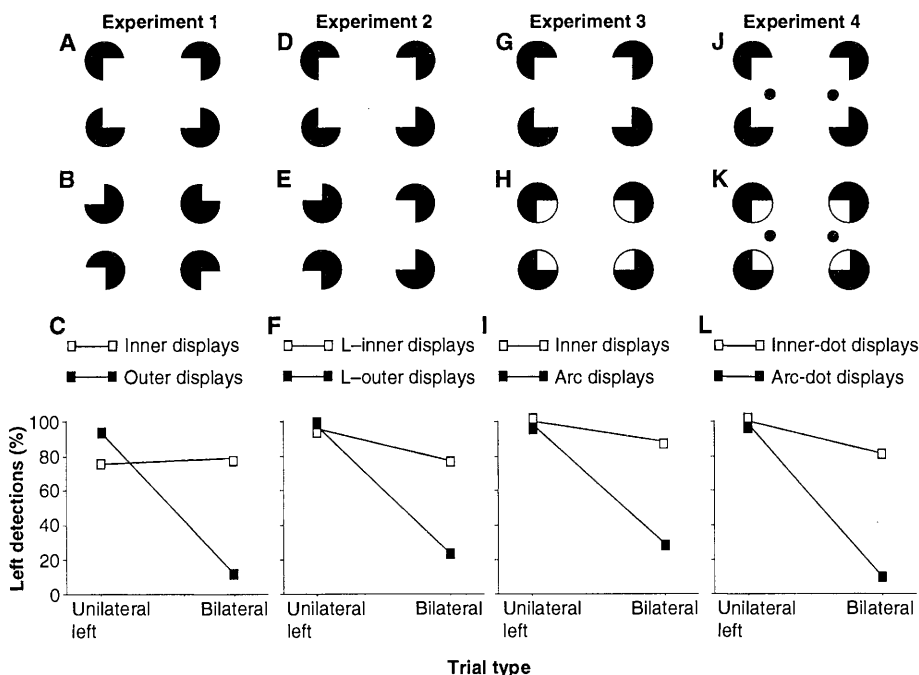


Fig. 3. Example displays (to scale) from bilateral trials in experiment 1 (A and B); experiment 2 (D and E); experiment 3 (G and H); and experiment 4 (J and K); with graphs below (C, F, I, and L) showing the relative magnitude of V.R.'s visual extinction for the two display types shown above (21). (C) Results for inner (A) and outer (B) displays in experiment 1, giving the percentage of correct left-sided detections on unilateral left and bilateral trials. V.R. detected significantly more left segments in inner bilateral trials [25 out of 32 (25/32)] than in outer bilateral trials (4/32, $P < 0.001$). (F) Results for left-inner (D) and left-outer (E) displays in experiment 2; V.R. detected significantly more left segments in left-inner bilateral trials (37/48) than in left-outer bilateral trials (11/48, $P < 0.001$). (I) Results for inner (G) and arc (H) displays in experiment 3; V.R. detected significantly more left segments in inner bilateral trials (28/32) than in arc bilateral trials (9/32, $P < 0.001$). (L) Results for inner-dot (J) and arc-dot (K) displays in experiment 4; V.R. detected significantly more left dots in bilateral trials for inner-dot displays (26/32) than for arc-dot displays (3/32, $P < 0.001$); see (22) for data from unilateral trials and catch trials.

tage for ipsilesional events over simultaneous contralesional events arising only between separate objects at attentive levels of vision. This deficit is ameliorated when preattentive processes derive a single subjective surface over which attention can then spread, in the manner recently suggested for normal people (12).

It might be objected, however, that instead of spreading across a subjective surface, V.R.'s impaired attention merely spreads from one inducing Pac-man to any other Pac-man that groups with it (14), with no implications for the physically empty space between them. This possibility was examined in experiment 4. Instead of reporting removed segments, V.R. was now required to detect the onset of dots that appeared between the inducing Pac-men, in the region encompassed by any subjective surface (Fig. 3J). The segments were either arranged to produce a Kanizsa rectangle enclosing any dots (Fig. 3J) or had arcs across them to veto the subjective surface (Fig. 3K). V.R. missed fewer left members of bilateral dot pairs in displays yielding a Kanizsa rectangle than in displays where there was no subjective figure (see graph in Fig. 3L).

These findings extend those of experiments 1 through 3 to confirm that V.R.'s attention does indeed spread across preattentively derived subjective surfaces, when these appear abruptly. As a result, her attention captures any visual information (such as the dots) that falls on these new surfaces, rather than merely grouping aligned Pac-men together. This surface interpretation receives further support from V.R.'s spontaneous reports of seeing "a big

white rectangle" suddenly appear, in bilateral inner trials only.

Our final experiment tested whether this influence of perceptual filling-in on extinction arises at the level of a 3D representation of visual surfaces. We used displays like those shown in Fig. 4, A through C. V.R.'s task was to detect the onset of black bars on either side of a central cube. In bilateral trials, the two bars were arranged pictorially to give the appearance of a single rod partially occluded by the cube (Fig. 4A), of two separate bars appearing just above the cube (Fig. 4B), or of two separate bars appearing in front of the cube (Fig. 4C).

V.R. showed significantly less extinction in the occlusion condition of experiment 5 (see graph in Fig. 4D), revealing that preserved processes of depth interpretation led to normal amodal completion of the two bars as part of a single occluded rod. She spontaneously commented that in this condition only, a single black stick appeared to "shoot behind the box" from right to left. This powerful influence of 3D interpretation is a radically new finding for extinction, which has previously been characterized as an entirely 2D phenomenon. The results accord with recent models of normal function (12), which emphasize that attention applies to surfaces within a depth interpretation rather than to 2D regions in a spatial map of image features, and which also argue (10) that completion of partially occluded surfaces can arise in preattentive vision, as confirmed by our neuropsychological findings in patient V.R.

The present results extend a previous report (14) that visual extinction is reduced when bilateral events can be grouped to-

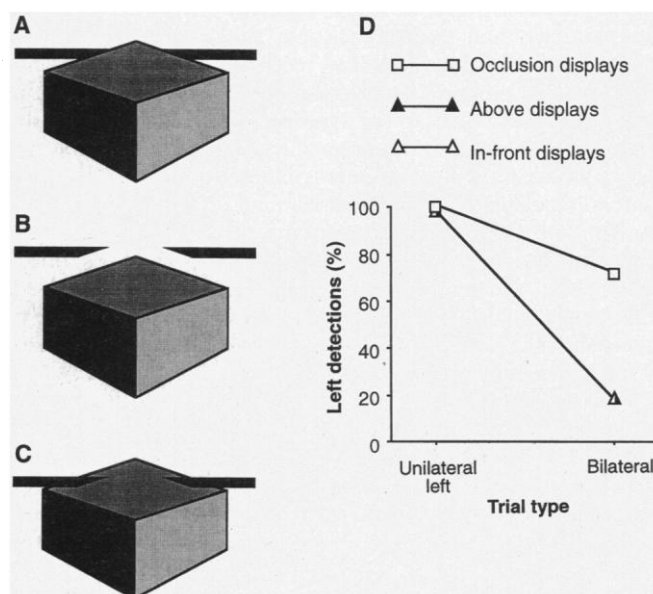
gether. That study only examined grouping by 2D alignment. This factor was equivalent across all control and experimental conditions in each of the present studies, so our results cannot be explained in such 2D terms alone. Instead, they show for the first time that visual extinction can operate at the level of a depth interpretation involving perceptually filled-in surfaces.

Our findings also show that V.R.'s extinction is not due to weak preattentive coding of image features for contralesional visual inputs. Whether contralesional events reached awareness or not after bilateral stimulation did not depend on the salience or position of these events as 2D blobs but on whether they formed a coherent new surface together with ipsilesional events. This was found even though the effective surfaces were incomplete in the retinal image, requiring the filling-in processes that produce subjective figures or that complete partially occluded objects. Thus, V.R.'s deficit evidently arises only in attentive vision, after normal preattentive filling-in of surfaces. These results provide neuropsychological evidence in support of recent claims that visual filling-in is preattentive and that visual attention is surface-based (12). The results are also consistent with neurophysiological data showing that neurons at early levels of the primate cortical visual system are sensitive to illusory contours as well as to luminance-defined edges (15). Finally, our findings support recent proposals (12, 16) that surface-based representations may be the first level of coding to yield visual awareness.

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Fig. 4. Example displays (to scale) from bilateral trials for the three display types used in experiment 5 (23). (A) Occlusion. (B) Above. (C) In-front. The graph (D) shows the relative magnitude of V.R.'s visual extinction for these three display types. V.R. detected significantly more left bars in bilateral trials in the occlusion condition (23/32), where such bars appeared to be one end of a single continuous rod running behind the cube [as in (A)], as compared with the control conditions [6/32 for the above displays (B) and 6/32 for the in-front displays (C); $P < 0.001$ for both comparisons with the occlusion condition]. Note that data from unilateral left and bilateral trials in above and in-front displays were identical (24).



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 13. For several reasons, V.R. is an ideal case for testing our hypothesis that the processes underlying visual filling-in will remain intact in parietal extinction. First, her lesion is primarily cortical, but she has no visual field cuts. The clinical phenomenon of extinction can be observed in several kinds of neurological patients but may arise for different reasons after the occurrence of distinct lesions [such as partial sensory loss (4) in patients with subcortical lesions]. Patients with mainly cortical damage (like V.R.) show deficits that are more attentional in nature and therefore provide the critical test for our present hypothesis; however, unlike V.R., many cortical patients have visual field cuts that render them unsuitable for our tests. Second, the large extent of V.R.'s cortical lesion places considerable constraints on the neural substrate for the preserved visual filling-in that we find within the intact tissue. Finally, although extinction is relatively common for a brief period after unilateral brain damage, it is often transient. In this respect, V.R. is also a particularly useful case; her disorder remained stable over many months, permitting the extensive testing documented here.
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 17. V.R.'s small left-hemisphere lesion had occurred 2 years before the right-hemisphere stroke, causing a transient right-sided homonymous hemianopia which resolved completely and no other symptoms. At the time of the present investigations, V.R. had full visual fields. There was no evidence of unilateral left neglect when conventional measures were used, including line-bisection and cancellation tasks; but V.R. showed consistent extinction of contralateral stimuli in the visual, tactile, and auditory modalities on confrontation. The experiments reported here were conducted between 1 and 24 months after the right-hemisphere stroke.
 18. All stimuli were displayed on the active matrix screen of a Macintosh PowerBook 540, controlled by VScope software [J. T. Enns and R. A. Rensink, *VScope Software Manual: Vision Testing Software for the Macintosh* (Micropsych Software, University of British Columbia, Vancouver, Canada, 1992)]. The viewing distance was 50 cm. Circular inducers were 5.1° in diameter, with a center-to-center separation of 10.2° horizontally and 7.4° vertically (all drawings are to scale, so that other visual angles may be derived).
 19. The duration for which the target segments were removed was determined before each experiment by a titration procedure aimed at producing 75% correct detections for unilateral left trials. This duration was 500 ms in experiment 1, 100 ms in experiment 2, and 250 ms in experiment 3.
 20. Within each experiment, all the conditions were implemented during a single session and in counterbalanced order, to rule out any influences of practice or long-term recovery on the comparisons of interest.
 21. In experiments 1, 3, and 4, V.R. completed four blocks of 36 trials, the two possible display types being blocked with their order counterbalanced in an ABBA design. In experiment 2, V.R. completed six blocks of 36 trials in an ABBAAB design. Each block always contained 16 bilateral, 8 unilateral left, and 8 unilateral right trials for a particular display type, plus 4 catch trials, all in a random order.
 22. In experiment 1, V.R. detected 12 out of 16 (12/16) unilateral left events and 15/16 unilateral right events of the inner type; and 15/16 unilateral left plus 16/16 unilateral right events of the outer type. She correctly reported the absence of any target event on all catch trials. In experiment 2, V.R. detected 23/24 unilateral left events and 24/24 unilateral right events for left-inner displays; and 24/24 unilateral events (left and right) for left-outer displays. For both display types in experiment 3, she detected 16/16 unilateral events (left and right), and made no false-positive responses on catch trials; likewise for experiment 4.
 23. The sequence of events in each trial was similar to that in experiments 1 through 4. A central fixation cross was displayed for 500 ms. This was replaced by a pictured cube (maximum height 10.8°, maximum width 14.6°) with perspective and shading cues constructed to yield a 3D shape. The "nearest" vertical edge of the cube appeared at the center of the screen, in line with fixation. One second later, a black horizontal bar appeared for 150 ms to the left or right of the cube (unilateral trials); or two bars appeared simultaneously for 150 ms on either side (bilateral trials, as illustrated); or no bars appeared (catch trials). The cube remained visible until V.R. reported whether there had been any bar on the right, left, both sides, or neither side. Each block of trials had the same structure as previously. The three display types were blocked in an ABCCBA order.
 24. For all three display types in experiment 5, V.R. detected every unilateral stimulus on the left and right and correctly reported the absence of any bars on all catch trials.
 25. We thank V.R. for her willing participation. J.B.M. was supported by a National Health and Medical Research Council (Australia) Neil Hamilton Fairley Fellowship, G.D. by the Biotechnology and Biological Sciences Research Council (UK), and J.D. by the Wellcome Trust (UK). We thank J. Bradshaw, J. Duncan, J. Pierson, I. Robertson, C. Rorden, and S. Tripathy for comments on the manuscript.

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NMDA Channel Regulation by Channel-Associated Protein Tyrosine Kinase Src

Xian-Min Yu, Rand Askalan, Gary J. Keil II, Michael W. Salter*

The *N*-methyl-D-aspartate (NMDA) receptor mediates synaptic transmission and plasticity in the central nervous system (CNS) and is regulated by tyrosine phosphorylation. In membrane patches excised from mammalian central neurons, the endogenous tyrosine kinase Src was shown to regulate the activity of NMDA channels. The action of Src required a sequence [Src(40–58)] within the noncatalytic, unique domain of Src. In addition, Src coprecipitated with NMDA receptor proteins. Finally, endogenous Src regulated the function of NMDA receptors at synapses. Thus, NMDA receptor regulation by Src may be important in development, plasticity, and pathology in the CNS.

The NMDA receptor is a principal subtype of ionotropic excitatory amino acid receptor that plays a central role in development, neuroplasticity, and excitotoxicity in the CNS (1). The function of NMDA receptor is regulated by protein phosphorylation at serine or threonine (2) and at tyrosine (3, 4) residues. For serine or threonine kinases, protein kinase C is an endogenous kinase (5) that regulates NMDA channel function. In contrast, the endogenous tyrosine kinase that regulates NMDA channels has been elusive. Numerous receptor (6), as well as nonreceptor (7), tyrosine kinases are expressed in the CNS. We set out to identify the endogenous tyrosine kinase regulating NMDA channel function.

We recorded NMDA receptor single-channel currents using inside-out patches taken from cultured rat central neurons (8). To investigate whether the endogenous ty-

rosine kinase was a nonreceptor tyrosine kinase in the Src family, we made use of a high-affinity peptide, EPQ(pY)EEIPIA (9), which activates this family of kinases. The nonphosphorylated form of the peptide, EPQYEEIPIA, is inactive (9) and was used as a control. Application of EPQ(pY)-EEIPIA to the cytoplasmic side of the membrane produced an increase in the channel activity (10) while having no effect on single-channel conductance (Fig. 1A). On average, channel open probability (P_o) increased to $260 \pm 38\%$ of the control value (mean \pm SEM; $n = 7$ patches), and there was an increase in mean open time to $152 \pm 18\%$. Peptide EPQ(pY)EEIPIA caused marked changes in the distribution of open and shut times (Fig. 1A), with alterations in the relative area of the components and no significant changes in the values of the time constants. In the distribution of open times, the area of the longest component was increased. For shut times, the area of the shortest component increased and that of the longest component decreased. Peptide EPQ(pY)EEIPIA also

Division of Neuroscience, Hospital for Sick Children, Department of Physiology, University of Toronto, Toronto, Ontario, M5G 1X8 Canada.

*To whom correspondence should be addressed.
E-mail: mike.salter@utoronto.ca