Ongoing in Vivo Experience Triggers Synaptic Metaplasticity in the Neocortex

Roger L. Clem,[1] Tansu Celikel,[2]* Alison L. Barth[1]†

In vivo experience can occlude subsequent induction of long-term potentiation and enhance long-term depression of synaptic responses. Although a reduced capacity for synaptic strengthening may function to prevent excessive excitation, such an effect paradoxically implies that continued experience or training should not improve and may even degrade neural representations. In mice, we examined the effect of ongoing whisker stimulation on synaptic strengthening at layer 4-2/3 synapses in the barrel cortex. Although *N*-methyl-D-aspartate receptors were required to initiate strengthening, they subsequently suppressed further potentiation at these synapses in vitro and in vivo. Despite this transition, synaptic strengthening continued with additional sensory activity but instead required the activation of metabotropic glutamate receptors, suggesting a mechanism by which continued experience can result in increasing synaptic strength over time.

N-methyl-D-aspartate receptor–dependent synaptic strengthening is the most common and best-understood form of plasticity in the central nervous system, found in brain areas ranging from the hypothalamus to the cerebral cortex and in species including amphibians, birds, and mammals. Because NMDARs are required for both learning in vivo and synaptic potentiation in vitro, it is likely that synaptic strengthening that occurs during the course of normal behavioral experience requires NMDARs (*1*). The occlusion of NMDAR-dependent long-term potentiation (LTP) after in vivo experience has been taken as evidence that the signaling pathways employed in behaving animals to increase synaptic strength are the same as those underlying LTP (*2*–*4*).

How NMDARs influence plasticity after the initiation of synaptic strengthening in vivo has not been well studied. Because experience-dependent plasticity is cumulative over time in many behaviorally relevant contexts, understanding how synaptic plasticity is modified or enhanced after its induction is critical to our ability to understand and facilitate learning (*5*). These questions may be especially important in the context of development and the maturation of sensory responses.

In slices from control mice, pairing-induced potentiation of cortical layer 4-2/3 synapses in vitro is NMDAR-dependent [Fig. 1A; protocol modified from (*6*); control, percent of baseline excitatory postsynaptic current (EPSC) amplitude: 162.5 ± 21.2%, n = 18 cells; + D,L-2-amino-5-phosphonovaleric acid (APV) 114.5 ± 8.8%, n = 10 cells; a scatter plot of all LTP experiments is shown in fig. S1]. This LTP was accompanied by an increase in AMPAR-EPSC rectification that lasted for the duration of recording (>30 min after induction; fig. S2), suggesting that it is accompanied by an increase in current through glutamate receptor 2–lacking, Ca^{2+}-permeable AMPA receptors (CP-AMPARs). Single-whisker experience (SWE), in which all but a single large facial whisker have been removed from the animal's snout (*7*, *8*), induces synaptic potentiation by CP-AMPAR addition to layer 4-2/3 synapses after 24 hours (*7*). Using c*fos*–coupled green fluorescent protein (fosGFP) transgenic mice to visualize the location of the spared whisker barrel (*9*), we examined whether synaptic potentiation could occur when NMDARs were blocked during SWE.

The competitive NMDAR antagonist carboxypiperazin-4-yl-propyl-1-phosphonic acid (CPP) has been used to block NMDARs in vivo (*10*, *11*). Although NMDAR antagonists can have sedative effects that might reduce levels of activity reaching the cortex and thereby influence SWE plasticity, we found that CPP injection did not alter whisker-evoked responses in vivo but did confer a mild motor impairment in control undeprived animals (fig. S3).

Animals injected with CPP throughout SWE (–2 hours and +12 hours after SWE onset) showed no increase in the ratio of AMPAR- to NMDAR-mediated EPSCs (A:N) versus control (Fig. 1, E to G; A:N ratio: control 1.01 ± 0.08, n = 11 cells; SWE 1.69 ± 0.12, n = 9 cells; SWE + CPP 1.01 ± 0.16, n = 6 cells). Additionally, the amplitude of quantal AMPAR-EPSCs (Sr^{2+}-mEPSC, in which Sr^{2+} was used to induce asynchronous glutamate release) was unchanged in animals receiving CPP (Fig. 1, H to J; Sr^{2+}-mEPSC amplitude: control 9.79 ± 0.35 pA, n = 11 cells; SWE 12.0 ± 0.46 pA, n = 10 cells; SWE + CPP 10.6 ± 0.39 pA, n =

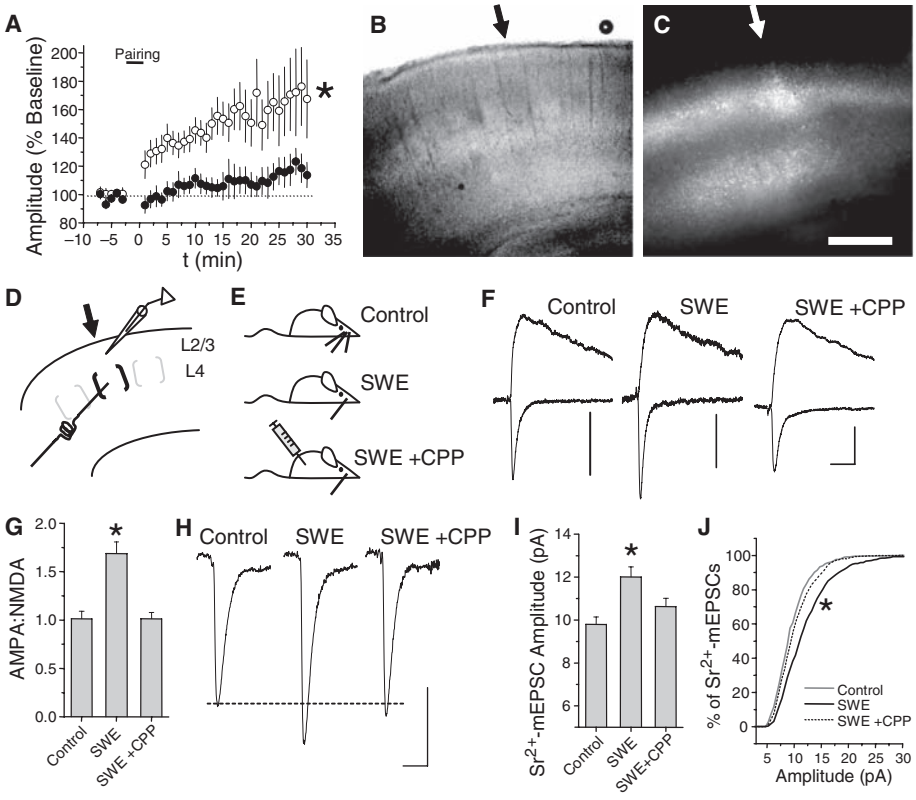

Fig. 1. LTP and SWE-induced synaptic strengthening require NMDARs. (**A**) Pairing (0 mV, 2 Hz, 360 pulses) induces LTP at layer 4-2/3 synapses from control undeprived mice (white circles) that is abolished in APV-treated cells (black circles). *t*, time. *P < 0.01. (**B**) Coronal slice of the barrel cortex under brightfield illumination. (**C**) Fluorescence illumination of (B) showing fosGFP expression in the spared barrel column (arrow). Scale bar, 500 μm. (**D**) Electrode positions. (**E**) Experimental groups for (F) to (J): control, whisker intact; SWE, 24 hours of SWE; SWE + CPP, 24 hours of SWE with recurrent CPP treatment. (**F**) Representative EPSCs at membrane holding potential (V_h) = –70 mV and +40 mV, scaled to +40 mV. Scale bars, 25 pA, 20 pA, and 25 pA × 20 ms, respectively. (**G**) Mean A:N ratio for all groups. *P < 0.001. (**H**) Group-averaged quantal Sr^{2+}-mEPSCs. Scale bar, 5 pA × 5 ms. (**I**) Mean Sr^{2+}-mEPSC amplitude. *P < 0.001. (**J**) Cumulative histogram of Sr^{2+}-mEPSC amplitude for all groups. *P < 0.001.

[1]Department of Biological Sciences and Center for the Neural Basis of Cognition, Carnegie Mellon University, Pittsburgh, PA 15213, USA. [2]Department of Cell Physiology, Max Planck Institute for Medical Research, Jahnstrasse 29, 69120 Heidelberg, Germany.

*Present address: Laboratory of Neural Circuits and Plasticity, University of Southern California, 3641 Watt Way, HNB 501, Los Angeles, CA 90089-2520, USA.

†To whom correspondence should be addressed. E-mail: barth@cmu.edu

12 cells). Despite the fact that in vitro LTP and in vivo synaptic strengthening occur over different time courses and may take advantage of different cellular mechanisms, these data indicate that both processes require NMDAR activation.

A common test of whether LTP-like processes have occurred in vivo is to see whether after in vivo stimulation, LTP can still be induced by artificial stimuli (*2*–*4*). If the intracellular pathways used to induce synaptic strengthening were maximally activated by in vivo experience, then further LTP should be difficult or impossible to elicit, a result that has been observed in previous studies (*2*–*4*). However, the mechanisms underlying LTP suppression and its physiological relevance remain poorly understood.

After 24 hours of SWE, pairing was no longer effective in inducing LTP and instead produced a mild depression at spared column layer 4-2/3 synapses in vitro (Fig. 2, D to F; 84.0 ± 5.5%, n = 7 cells). These data suggest that, coincident with an increase in quantal AMPAR-mediated EPSC amplitude (*7*), in vivo experience saturates or fundamentally alters NMDAR-dependent LTP at these synapses. The magnitude of LTP of deprived 4-2/3 synapses was similar to that of the control (Fig. 2, B and F; 150.2 ± 9.7%, n = 8 cells) and was eliminated after treatment with APV (Fig. 2, C and F; 97.1 ± 5.8%, n = 7 cells).

Because we observed a mild depression of synaptic responses after pairing in the spared column, it seemed possible that NMDAR activation induced long-term depression (LTD), a possible homeostatic response to the saturation of synaptic strengthening (*5*). Unexpectedly, APV application revealed a strong potentiation of spared column 4-2/3 synapses (Fig. 3, B and F; 179.1 ± 31.2%, n = 8 cells). This result indicated that LTP was not merely saturated at these synapses but NMDARs had acquired the ability to suppress pairing-induced synaptic strengthening in vitro.

We next sought to characterize this NMDAR-independent form of LTP at layer 4-2/3 synapses in the spared column. In the presence of APV, inclusion of the Ca^{2+} chelator BAPTA (10 mM) in the recording electrode blocked LTP (Fig. 3, C and F; 91.3 ± 3.7%, n = 7 cells), indicating that potentiation requires postsynaptic Ca^{2+} entry. At excitatory synapses onto interneurons (*12*, *13*), as well as at glutamatergic contacts on some glial cells (*14*), activation of CP-AMPARs is required for LTP. Previous work has shown that these receptors are trafficked to and maintained at layer 4-2/3 synapses by sensory-evoked activity in the spared barrel column (*7*). Thus, it was conceivable that this Ca^{2+}-dependent form of NMDAR-independent LTP required activation of CP-AMPARs. However, pharmacological blockade of CP-AMPARs with the specific antagonists philanthotoxin-433 (PhTX) or joro spider toxin (JsTX) did not reduce LTP induced at spared 4-2/3 synapses treated with APV (Fig. 3, D and F; 167.3 ± 22.7%, n = 5 cells, pooled).

Metabotropic glutamate receptor (mGluR) activation can support LTP in some types of interneurons (*15*, *16*) and at excitatory synapses in the cerebellum (*17*), amygdala (*18*), and hippocampus (*19*, *20*), although it usually complements NMDAR-mediated plasticity. In order to investigate whether these receptors might be responsible for the APV-resistant LTP in the spared barrel column, we bath-applied the broad-spectrum mGluR antagonist MCPG [(RS)-α-methyl-4-carboxyphenylglycine] together with APV. Under these conditions, pairing-induced LTP was fully eliminated (Fig. 3, E to F; MCPG + APV, 95.2 ± 3.3%, n = 8 cells). Thus, after the onset of experience-dependent plasticity in the spared barrel column, mGluRs can oppose NMDAR-mediated synaptic depression in vitro.

These experiments indicate that, at least in brain slices for pairing-induced LTP, the rules governing the induction of synaptic strengthening are altered by sensory experience. Does this switch in

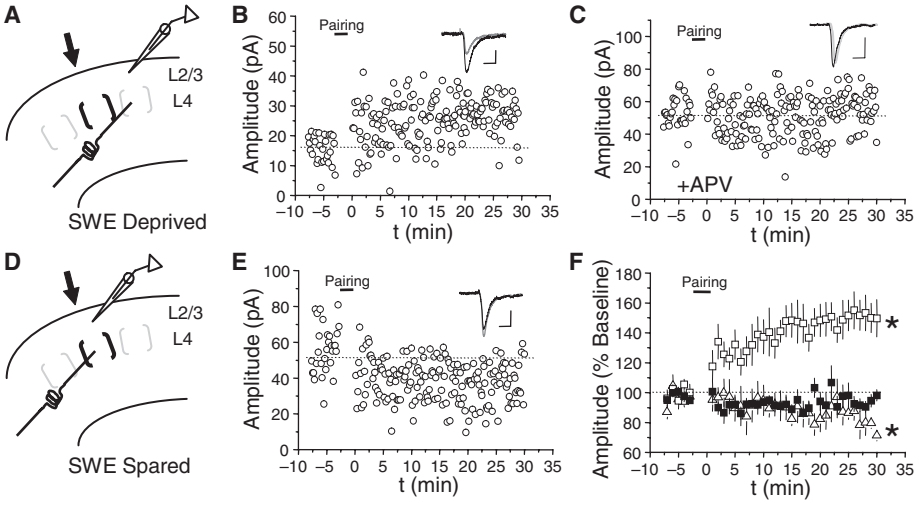

Fig. 2. SWE occludes pairing-induced LTP in vitro. (**A** and **D**) Electrode positions for recording in deprived (A) or spared (D) columns. (**B** and **C**) Representative experiments showing pairing-induced LTP in a deprived column (B) that is abolished in APV-treated cells (C). Inset in (B), (C), and (E) shows averaged EPSC before pairing (gray) and 30 min after pairing (black). Scale bar in (B), 10 pA × 10 ms; in (C), 20 pA × 10 ms. (**E**) Representative experiment showing that LTP is not elicited in the spared column. Scale bar, 30 pA × 10 ms. (**F**) Summary of LTP experiments at 4-2/3 synapses in spared (triangles), deprived (white squares), and deprived + APV (black squares) columns. $P < 0.01$.

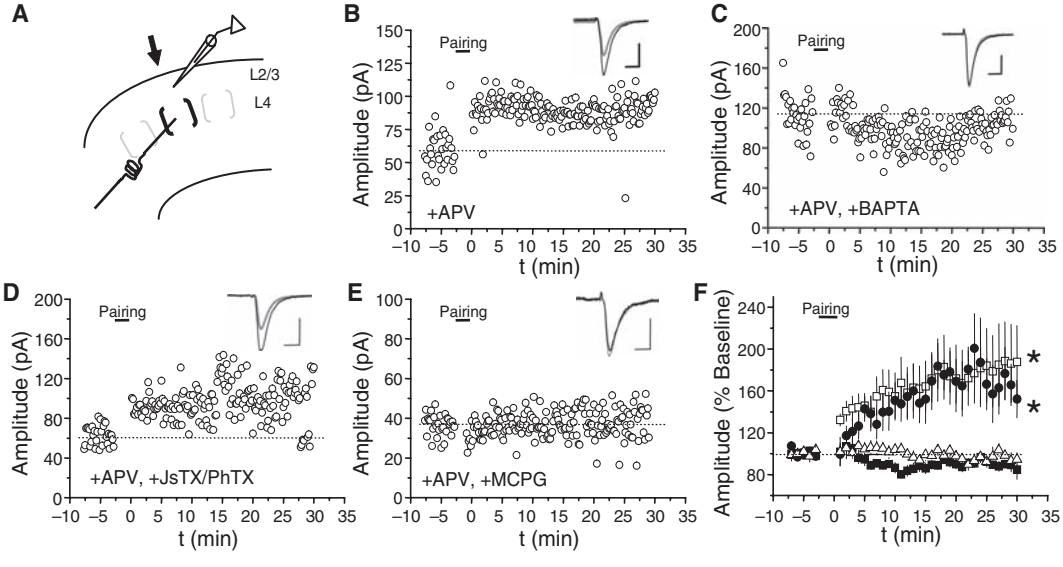

Fig. 3. NMDAR block reveals mGluR- and Ca^{2+}-dependent LTP at spared column synapses. (**A**) Electrode positions. (**B** to **E**) For pairing at 4-2/3 synapses within the spared column of slices from SWE animals, representative experiments for (B) APV, (C) APV + BAPTA, (D) APV + JsTX or PhTX (data pooled), and (E) APV + MCPG are shown. Scale bars in (B), 40 pA × 10 ms; in (C), 30 pA × 10 ms; in (D), 60 pA × 10 ms; in (E), 20 pA × 10 ms. (**F**) Summary of pairing-induced plasticity experiments. APV-only (white squares), APV + BAPTA (black squares), APV + PhTX or JsTX (black circles), and APV + MCPG (white triangles). *$P < 0.01$.

NMDAR function also occur in vivo, suppressing SWE-induced potentiation after its initial NMDAR-dependent induction? To address this, mice were subjected to 18 hours of SWE and then injected with CPP. At 24 hours after SWE onset (6 hours after CPP injection), acute brain slices were prepared and the properties of layer 4-2/3 synapses were assessed (Fig. 4A). The A:N ratio was significantly increased in CPP-treated as compared to SWE-only mice (Fig. 4, B and C; SWE/no drug 1.69 ± 0.12, $n = 9$ cells; SWE + CPP 2.24 ± 0.20, $n = 11$ cells; $P < 0.001$), and this increase could be attributed at least partly to an increase in Sr^{2+}-mEPSC amplitude (Fig. 4, D to F; spared/no drug 12.0 ± 0.46 pA, $n = 10$ cells; spared + CPP 13.98 ± 0.30 pA, $n = 14$ cells). Our results are consistent with at least one other study showing that NMDAR antagonists prevent the decay of LTP induced in vivo (*11*) and show that synaptic strengthening can be enhanced by precisely timed treatment with NMDAR antagonist.

In vivo treatment with the competitive mGluR group I antagonist 1-aminoindan-1,5-dicarboxylic acid (AIDA), 18 hours after the onset of SWE and 6 hours before slice preparation (Fig. 4A), resulted in the reduction of both the A:N ratio and Sr^{2+}-mEPSC amplitudes to control values (Fig. 4, B and C; A:N ratio: spared + AIDA 0.98 ± 0.07, $n = 9$ cells; Fig. 4, D to F; Sr^{2+}-mEPSC amplitude: spared + AIDA 9.56 ± 0.25 pA, $n = 11$ cells), indicating that mGluR activation is required at least for the maintenance of increased synaptic strength induced by in vivo sensory experience. Neither drug had any effect in control animals when administered 6 hours before animals were killed (Fig. 4, B and C; A:N ratio: control + CPP 1.02 ± 0.07, $n = 8$ cells; control + AIDA 1.02 ± 0.08, $n = 7$ cells; Fig. 4, D to F; Sr^{2+}-mEPSC amplitude: control + CPP 10.6 ± 0.26 pA, $n = 10$ cells; control + AIDA 10.12 ± 0.34 pA, $n = 9$ cells).

NMDAR subunit composition can be altered by sensory deprivation (*21*), with increased decay-time constants and heightened sensitivity to the NMDAR 2B subunit–specific antagonist ifenprodil at excitatory synapses (*7*, *22*). However, we found no evidence for an alteration in NMDAR properties at spared column layer 4-2/3 synapses with respect to decay kinetics, ifenprodil sensitivity, and current/voltage relations (fig. S3). Thus, the switch in NMDAR function probably occurs at the level of coupling to intracellular signaling cascades.

If NMDARs and mGluRs act simultaneously both to oppose and promote potentiation after its initiation, which process dominates with ongoing in vivo experience? To address this, we looked at the amplitude of quantal layer 4-2/3 AMPAR-EPSCs after 48 hours of SWE. Mean amplitude significantly increased with longer SWE treatment (48 hours of SWE: 14.25 ± 0.46 pA, $n = 12$ cells; versus 24 hours of SWE: 12.0 ± 0.46 pA, $n = 10$ cells; fig. S5). Thus, despite a switch in the ability of NMDARs to support potentiation, a physiologically relevant capacity for LTP is maintained in vivo, and cumulative experience can continue to increase synaptic strength. This augmentation probably depends on continued mGluR activation, because AIDA injection 6 hours before slice preparation abolished SWE-induced potentiation (Fig. 4, D to F).

These results do not rule out presynaptic modifications that could contribute to LTP or LTD in

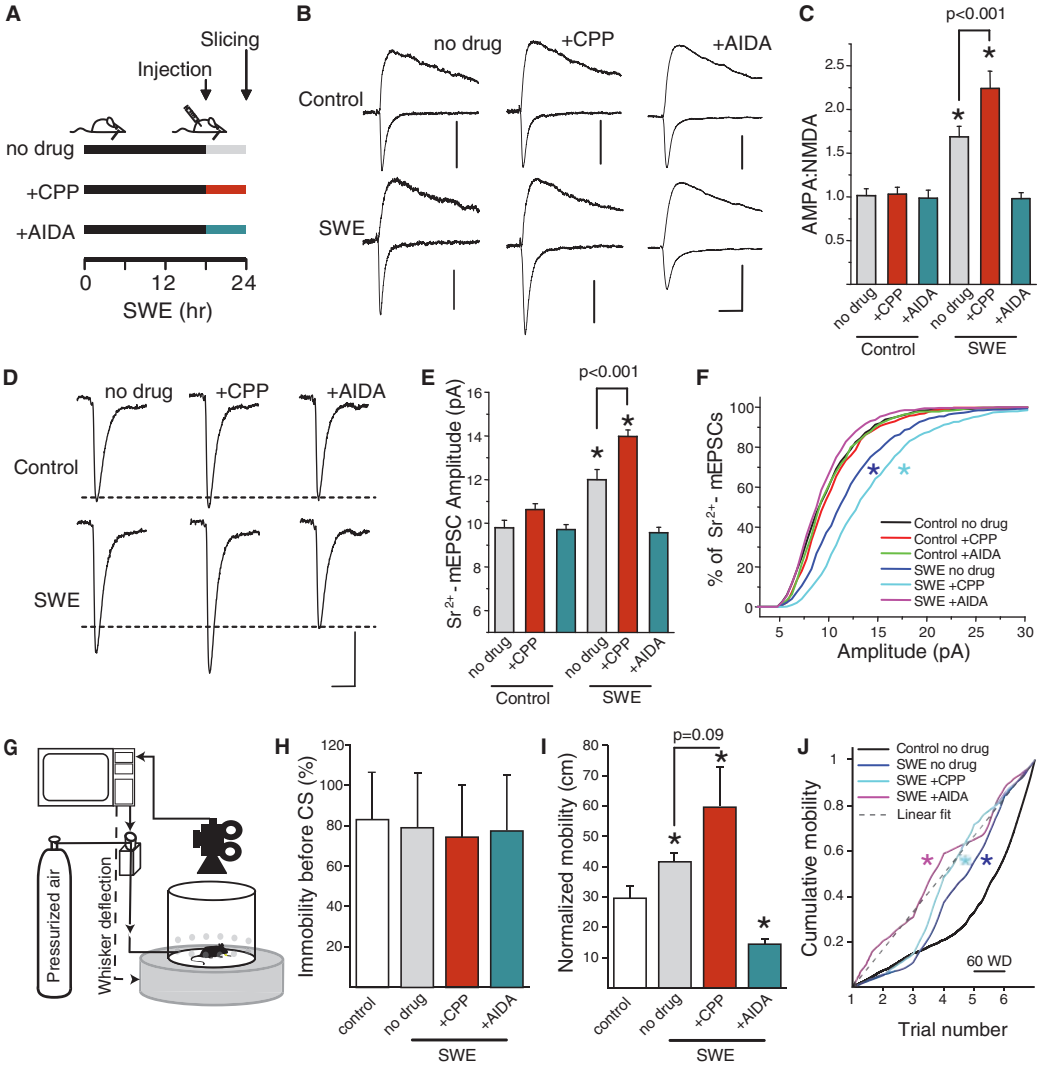

Fig. 4. NMDARs and mGluRs oppositely regulate synaptic strength and behavioral plasticity in vivo after SWE initiation. (**A**) Experimental timeline for joint SWE and in vivo drug delivery. CPP or AIDA was injected 18 hours after SWE onset. Slices were prepared 6 hours later. (**B**) Representative layer 4-2/3 EPSCs at $V_h = -70$ mV and +40 mV for each experimental group, scaled to peak current at +40 mV. Scale bars: control, 25 pA; control + CPP, 25 pA; control + AIDA, 40 pA; SWE spared, 20 pA; SWE spared + CPP, 30 pA; SWE spared + AIDA, 60 pA × 20 ms. (**C**) Mean A:N ratio for all groups. (**D**) Group-averaged Sr^{2+}-mEPSCs. Scale bar, 5 pA × 10 ms. (**E**) Mean Sr^{2+}-mEPSC amplitude. (**F**) Cumulative histogram of Sr^{2+}-mEPSC amplitude. *$P < 0.001$ versus control. (**G**) Experimental setup for associative tactile conditioning. Whisker deflections [CS, 100 ms (up) and 400 ms (down) at 2 Hz for 30 s] were paired with air-puff stimuli (US, 3 bars, 5 s overlapping with last 5 s of CS), and animal mobility was quantified from video recordings during conditioning by custom-written software. As animals learned to associate the whisker deflections with the air-puff stimuli, they tended to increase their mobility to avoid the upcoming US. (**H**) Fraction of time spent immobile in test chamber immediately before CS onset did not differ between test groups, indicating that whisker deprivation or drug treatment did not influence mobility. (**I**) Animal mobility normalized to movement before CS. *$P < 0.05$ versus control. (**J**) Cumulative distribution of mobility over all trials shows that SWE mice learned faster than controls and that SWE + CPP mice learned faster than SWE and control animals. SWE + AIDA animals failed to acquire the task, with equal mobility responses for each training trial (linear fit for cumulative mobility). *$P < 0.01$ for all pairwise comparisons across groups.

vitro (*23*); however, increased quantal amplitude after SWE and pharmacological treatments in vivo identify a clear postsynaptic component for the plasticity observed. Although the in vitro pairing protocol is a crude approximation of the kind of activity that layer 2/3 neurons experience in vivo, it combines a physiological frequency (*24*, *25*) of afferent stimulation (2 Hz) with NMDAR activation and predicts with remarkable accuracy the effects of in vivo SWE and pharmacological treatment.

Is this increase in synaptic strength correlated with learning behavior? To test this, we used an associative tactile conditioning task that pairs whisker deflection [conditioned stimulus (CS)] with a nonaversive, habituating air-puff stimulus [unconditioned stimulus (US); Fig. 4G and movies S1 and S2]. SWE mice showed increased mobility after whisker deflection as compared to controls, indicating that the SWE enhanced CS-US association (Fig. 4I). In parallel with their effects on synaptic strength in SWE mice, treatment with CPP and AIDA further enhanced or reduced associative learning (Fig. 4I). Analysis of changes in mobility over the course of task acquisition shows that SWE + CPP–treated animals acquired the CS-US association significantly faster than did SWE animals (Fig. 4J). These data indicate that increased synaptic strength in the barrel cortex is associated with enhanced performance in a whisker-dependent learning task, and that NMDAR and mGluR antagonists similarly affect synaptic strength and behavioral output.

Why doesn't normal sensory experience (that is, when all whiskers are intact) result in a similar occlusion of NMDAR-dependent LTP? Compared to SWE, this stimulus may not be sufficiently strong to induce a switch in NMDAR and mGluR properties. However, in both our experiments and many others [see, for example (*26*, *27*)], a fraction of neurons failed to demonstrate NMDAR-dependent LTP. It is tempting to speculate that in these cells, an mGluR-dependent form of LTP might be observed in the presence of NMDAR antagonists.

Our results indicate that after the initiation of LTP-like processes by sensory experience, a capacity for further synaptic strengthening is preserved and depends on mGluR activation. Because mGluR-mediated synaptic strengthening was observed both in vitro and in vivo, this is likely to be a physiologically relevant mechanism that may explain why an apparent "ceiling" for LTP does not negate the benefits of cumulative experience in enhancing response properties in the neocortex.

References and Notes

1. R. C. Malenka, M. F. Bear, *Neuron* **44**, 5 (2004).
2. M. S. Rioult-Pedotti, D. Friedman, J. P. Donoghue, *Science* **290**, 533 (2000).
3. B. Sacchetti *et al.*, *Eur. J. Neurosci.* **15**, 143 (2002).
4. J. R. Whitlock, A. J. Heynen, M. G. Shuler, M. F. Bear, *Science* **313**, 1093 (2006).
5. W. C. Abraham, W. P. Tate, *Prog. Neurobiol.* **52**, 303 (1997).
6. N. Hardingham *et al.*, *J. Neurosci.* **23**, 4428 (2003).
7. R. L. Clem, A. Barth, *Neuron* **49**, 663 (2006).
8. S. Glazewski, B. L. Benedetti, A. L. Barth, *J. Neurosci.* **27**, 3910 (2007).
9. A. L. Barth, R. C. Gerkin, K. L. Dean, *J. Neurosci.* **24**, 6466 (2004).
10. C. Kentros *et al.*, *Science* **280**, 2121 (1998).
11. D. M. Villarreal, V. Do, E. Haddad, B. E. Derrick, *Nat. Neurosci.* **5**, 48 (2002).
12. J. G. Gu, C. Albuquerque, C. J. Lee, A. B. MacDermott, *Nature* **381**, 793 (1996).
13. N. K. Mahanty, P. Sah, *Nature* **394**, 683 (1998).
14. W. P. Ge *et al.*, *Science* **312**, 1533 (2006).
15. C. J. McBain, T. J. DiChiara, J. A. Kauer, *J. Neurosci.* **14**, 4433 (1994).
16. Y. Perez, F. Morin, J. C. Lacaille, *Proc. Natl. Acad. Sci. U.S.A.* **98**, 9401 (2001).
17. E. D'Angelo, P. Rossi, S. Armano, V. Taglietti, *J. Neurophysiol.* **81**, 277 (1999).
18. O. Lee, C. J. Lee, S. Choi, *Neuroreport* **13**, 685 (2002).
19. Z. I. Bashir *et al.*, *Nature* **363**, 347 (1993).
20. Y. M. Lu *et al.*, *J. Neurosci.* **17**, 5196 (1997).
21. E. M. Quinlan, D. H. Olstein, M. F. Bear, *Proc. Natl. Acad. Sci. U.S.A.* **96**, 12876 (1999).
22. B. D. Philpot, A. K. Sekhar, H. Z. Shouval, M. F. Bear, *Neuron* **29**, 157 (2001).
23. V. A. Bender, K. J. Bender, D. J. Brasier, D. E. Feldman, *J. Neurosci.* **26**, 4166 (2006).
24. T. Celikel, B. Sakmann, *Proc. Natl. Acad. Sci. U.S.A.* **104**, 1395 (2007).
25. T. Celikel, V. A. Szostak, D. E. Feldman, *Nat. Neurosci.* **7**, 534 (2004).
26. A. L. Barth, R. C. Malenka, *Nat. Neurosci.* **4**, 235 (2001).
27. C. C. Petersen, R. C. Malenka, R. A. Nicoll, J. J. Hopfield, *Proc. Natl. Acad. Sci. U.S.A.* **95**, 4732 (1998).

28. Research was supported by grant DA017188-01 from the National Institutes of Health. We thank B. Benedetti for in vivo recording data and P. Castillo, M. Wheeler, and K. Velanova for helpful discussions.

Supporting Online Material

www.sciencemag.org/cgi/content/full/319/5859/101/DC1
Materials and Methods
Figs. S1 to S6
References
Movies S1 and S2

16 April 2007; accepted 2 November 2007
10.1126/science.1143808

Small Circuits for Large Tasks: High-Speed Decision-Making in Archerfish

Thomas Schlegel and Stefan Schuster*

The enormous progress made in functional magnetic resonance imaging technology allows us to watch our brains engage in complex cognitive and social tasks. However, our understanding of what actually is computed in the underlying cellular networks is hindered by the vast numbers of neurons involved. Here, we describe a vertebrate system, shaped for top speed, in which a complex and plastic decision is performed by surprisingly small circuitry that can be studied at cellular resolution.

It is widely accepted that cognitive abilities such as making complex decisions require the enormous densities of highly interconnected cortical neurons. However, not all neurons within the areas labeled by functional magnetic resonance imaging (fMRI) as active during complex cognitive tasks [e.g., (*1*–*4*)] might be crucial for the performance, and perhaps much smaller "minimum circuitry" would suffice. Here, we provide evidence for this view in a vertebrate system, in which a highly complex decision is made by surprisingly compact neural circuitry.

Archerfish are renowned for their ability to down aerial insect prey with precisely aimed shots of water. As soon as their successful shots dislodge their prey from the substrate, the fish must make an important decision (Fig. 1). On the basis of at least three independently varying initial parameters of prey motion, they must initiate an adapted open-loop start that, without requiring any further sensory information, rotates the fish toward where their prey will later land and pushes them off with a speed matched to distance (*5*–*7*). Due to heavy competition from peers and other surface-feeding fish, this decision must be made rapidly and accurately. The decision requires learning and is absent when competition is lacking, and its tuning appears to involve high levels of generalization and abstraction (*8*–*10*).

In principle, archerfish could use a priori information to prime and speed up their decisions: Observing the shot would signal all school members when aerial motion needs to be responded to and could perhaps even signal the likelihood of particular trajectories. To test the importance of such contextual information, we completely deprived the fish of it. In these experiments prey was initially invisible to the fish, and the experimenter could at any time elicit a prey trajectory with speed and angle randomly selected from large ranges (matching the corresponding ranges in naturally dislodged prey) (fig. S1). Surprisingly, even when shooting-related information was thus not available for priming the decisions, the minimum and average latencies required for accurate responses were not longer than in the control, and average latency appeared to be even slightly reduced (by about 5 ms, $P = 0.034$; Fig. 2B; table S1). Furthermore, with only target motion available, the fish were just as accurate as when additional contextual information was freely available ($P = 0.212$; Fig. 2C; table S1). These findings show that motion cues are necessary and sufficient to trigger the archerfish's high-speed decisions and this, in turn, places full control over all decision-relevant parameters in the hands of the experimenter.

Prospective shooters must precisely pinpoint the location of their aerial prey (*11*) and could thus focus

Universität Erlangen-Nürnberg Institut für Zoologie II, Staudtstrasse 5, D-91058 Erlangen, Germany.

*To whom correspondence should be addressed. E-mail: sschuste@biologie.uni-erlangen.de

Ongoing in Vivo Experience Triggers Synaptic Metaplasticity in the Neocortex

Roger L. Clem, Tansu Celikel, and Alison L. Barth

Science, 319 (5859), • DOI: 10.1126/science.1143808