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9. Oocytes (Dumont stage V-VI) were harvested (*20*) from adult female *X. laevis* under anesthesia [0.35% MS-222 (3-aminobenzoic acid ethyl ester), Sigma]. Theca and follicular layers were removed by incubation for 3 hours in Ca^{2+}-free and 82.5 m*M* NaCl ND-96 solution. Denuded oocytes were injected 1 to 24 hours later with 0.5 to 50 ng of mRNA (in 50 nl). Oocytes were incubated at 18°C for up to 120 hours in ND-96, which is 96 m*M* NaCl, 2 m*M* KCl, 1.8 m*M* $CaCl_2$, 1 m*M* $MgCl_2$, 2.5 m*M* sodium pyruvate, 0.5 m*M* theophylline, 5 m*M* Hepes, and gentamycin (50 μg/ml).
10. Recordings of membrane current were made 24 to 96 hours after injection of mRNA. Oocytes were continuously superfused (3 ml/min) with ND-96 (pyruvate, theophylline, and gentamycin omitted) at 23° to 25°C and were voltage-clamped with two microelectrodes (resistance 0.1 to 1 megohm) by using standard techniques [A. S. Finkel and P. W. Gage, in *Voltage and Patch Clamping with Microelectrodes*, T. G. Smith, H. Lecar, S. J. Redman, P. W. Gage, Eds. (Williams and Wilkins, Baltimore, 1985), pp. 47–94]. Single sweep current traces were low-pass filtered at 3 or 10 kHz before recording and are presented without leak subtraction. Oocytes (89%) displayed large K^+ currents 48 to 96 hours after injection of 25 to 100 ng of RBK-1 mRNA (two RNA preparations injected into 45 oocytes from four *Xenopus* donors). The outward current evoked by stepping from −90 (or −70) to −30 mV was 4.3 ± 0.45 μA (peak) and 3.1 ± 0.33 μA after 1 s (n = 30). Leak currents during these steps did not exceed 0.2 μA. No rapidly developing outward currents were observed in uninjected or water-injected oocytes (n = 44). As reported [N. Dascal, *CRC Crit. Rev. Biochem.* **22**, 317 (1987)], slowly developing outward currents were occasionally observed in uninjected oocytes during steps to −20 or 0 mV, but these did not exceed 0.1 μA and were not affected by tetraethylammonium (1 m*M*) or 4-AP (3 m*M*). The peak amplitude of the outward current was strongly related to the amount of mRNA injected. After 48 to 60 hours, the current evoked by stepping from −90 to −30 mV was 0.08 ± 0.06 μA (2 out of 8 positive) for 500 pg of mRNA, 0.82 ± 0.18 μA (12 out of 14 positive) for 5 ng of mRNA and 1.81 ± 0.37 μA (7 out of 8 positive) for 50 ng of mRNA.
11. For K^+ concentrations of 2 to 20 m*M*, the reversal potential of the tail current was measured by stepping to 0 mV for 10 ms and then measuring the current amplitude immediately after stepping back to different potentials. For 40, 60, and 80 m*M* K^+, reversal of the current was observed directly. NaCl was reduced when KCl was increased in these experiments, so the good agreement with the Nernst equation implies that Na^+ was not significantly permeable. The current was also unaffected by substituting isethionate for 90% of the Cl^- ions (n = 3).
12. The time constant for activation was 2.7 ± 0.3 ms at −20 mV, and 6.0 ± 1.3 ms at −40 mV (mean ± SEM, n = 5); measurements were inaccurate at 0 and +20 mV because currents may have been contaminated by capacitative transients. At the end of the depolarizing step the current declined with a time constant of 5.0 ± 0.3 ms (2 m*M* K^+, at −70 mV, n = 4). The faster time constants of inactivation during a sustained depolarization were 68.3 ± 8.4 ms at −40 mV, 36.5 ± 1.0 ms at −10 mV, and 43.9 ± 13.0 ms at +10 mV (n = 4); the slower time constants were 11.0 ± 2.3 s at −40 mV, 5.8 ± 1.4 s at −10 mV, and 10.8 ± 3.9 s at +10 mV (n = 4). Recovery from inactivation reached 60% ± 10% (n = 4) within 1 s and was complete between 30 and 60 s.
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Inescapable Versus Escapable Shock Modulates Long-Term Potentiation in the Rat Hippocampus

TRACEY J. SHORS, THOMAS B. SEIB, SEYMOUR LEVINE, RICHARD F. THOMPSON

A group of rats was trained to escape low-intensity shock in a shuttle-box test, while another group of yoked controls could not escape but was exposed to the same amount and regime of shock. After 1 week of training, long-term potentiation (LTP) was measured in vitro in hippocampal slices. Exposure to uncontrollable shock massively impaired LTP relative to exposure to the same amount and regime of controllable shock. These results provide evidence that controllability modulates plasticity at the cellular-neuronal level.

EXPOSURE TO INESCAPABLE SHOCK in laboratory animals has been linked to marked changes in endocrine activity and central nervous system neurochemistry (*1*), suppressed immunological function (*2*), increased gastric ulceration (*3*), reduced activity (*4*), weight loss (*5*), decreased aggression and lowered dominance status (*6*), and analgesia (*7*). Most of these effects can be ameliorated when the animal can control the aversive event; control is defined as the capacity to make an instrumental response to an aversive stimulus.

Of particular interest are the learning deficits observed after exposure to inescapable shock (*8*). These deficits cover a wide range of tasks (*9*) and are often transferred from one task to another (*10*). Similar regimes have a detrimental effect on LTP in the rat hippocampus (*11*). LTP is a form of neuronal plasticity characterized by an increase in synaptic response to a constant volley after brief tetanic stimulation of afferent fibers (*12*). Because of its relatively long time course, localization in the hippocampus (although not exclusively), and correlation with behavioral learning (*13–17*), LTP has been suggested as a component of associative memory formation (*18*).

Prior exposure to uncontrollable shock eliminated LTP in the in vitro hippocampal slice preparation (*11*). To determine whether this effect, like those described above, could be ameliorated by permitting the animal to exert control, we placed Long-Evans male rats (n = 12), weighing 200 to 250 g, and a second group of yoked controls (n = 12) in identical soundproof shuttle boxes. Boxes were linked to a scrambled-shock generator, and the rats were subjected to low-intensity shock (60 Hz, 1 mA) every minute for 30 min. Yoked controls could not escape, but experimental animals were able to escape by running through an archway (8 cm by 8 cm) and tripping a balance switch that shut off the current to the boxes of both groups simultaneously. After seven daily sessions of 30 shock presentations with an intertrial interval (ITI) of 60 s, the experimental group had mastered the behavior to the extent that the duration of each shock had dropped on average from 3.8 to 1.5 s and over 75% of the responses were less than 1.5 s (Fig. 1).

Immediately after the seventh morning of training, animals from both groups were killed and hippocampal slices (400 μm) were prepared (*19*). Twelve additional Long-Evans males were taken directly from their home cages and killed, and hippocampal slices were prepared. Trunk blood was collected from all rats for corticosterone radioimmunoassay (*20*). Recordings were performed "blind" by the experimenter.

Extracellular field potentials were recorded from the cell body layer of CA1 after pulsed stimulation of the Schaffer collateral branches of CA3 pyramidal cell axons. After a 10-min stability period, input-output functions were obtained. The potential before tetanus was set at one-half the maxi-

T. J. Shors, T. B. Seib, R. F. Thompson, Department of Psychology, University of Southern California, Los Angeles, CA 90089.
S. Levine, Department of Psychiatry, Stanford University, Stanford, CA 93405.

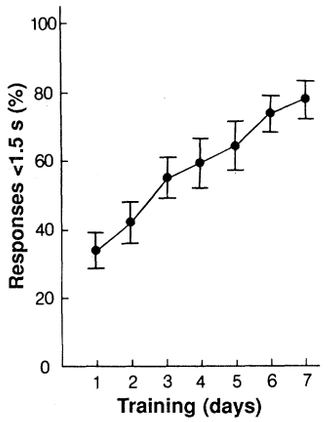

Fig. 1. Twelve rats and their yoked controls were given 30 shocks per day. The learning curve represents the mean percentage of escape responses (± SEM) that were <1.5 s for each day of training.

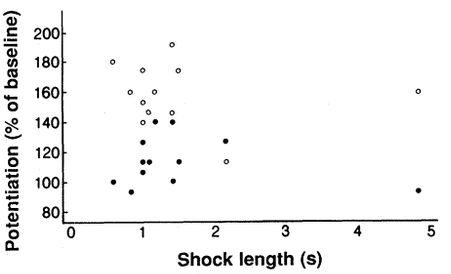

Fig. 2. The average length of one shock (1 mA, 60 Hz) for each rat on the last day of training is plotted against the potentiation obtained from that rat; ○, rats that could escape; ●, rats that could not escape.

mum response. A 100-Hz, 1-s tetanus was delivered, and potentials were monitored to 30 min after tetanus. Amplitudes were calculated from the mean of the first positive–first negative peak difference and the first negative–second positive peak difference. The change in amplitude after tetanus was averaged across slices for each rat, and potentiation was expressed as a percentage of the potential recorded before tetanus (*21*).

Mean potentiation (± SEM) at 30 min for the group that could escape was 156% (±6%) of the baseline, whereas potentiation for the group that could not escape was 111 ± 5%. The 12 animals not trained or shocked had a mean increase in potentiation of 189 ± 11%. Analysis of variance of the three groups [$F(2,33) = 24.96$, $P < 0.01$] and post-hoc Newman Keuls ($P < 0.05$) tests between the trained rats and their yoked controls revealed that exposure to inescapable shock resulted in significantly less potentiation 30 min after tetanus than exposure to the same number and duration of escapable shocks (Fig. 2). Comparing LTP from the escapable group and the unshocked controls revealed a significant decrement in the LTP of the escapable group ($P < 0.05$). In other words, exposure to shuttle-box escape training in itself resulted in a significant impairment of LTP (*22*).

We measured the mean potentiation of the three groups in 5-min intervals from tetanus to 30 min after tetanus (Fig. 3). The increase immediately after tetanus (within the first minute) is posttetanic potentiation (PTP), a short-lived increase in excitability thought to be due to increased presynaptic transmitter release, whereas the induction of LTP is considered to be in part postsynaptic (*23*). PTP occurred in all groups but was also significantly reduced [$F(2,33) = 5.18$, $P < 0.05$] in the yoked controls relative to the group that could escape ($P < 0.05$) and the unshocked controls ($P < 0.05$). No such effect occurred between the group that could escape and the unshocked controls.

There was no significant difference ($P > 0.05$) between the plasma corticosterone levels of the two shocked groups. The mean ± SEM for the group that could not escape was 59 ± 3 μg/dl and for the group that could escape was 63 ± 2 μg/dl. Thus, after 7 days of exposure to shock, the corticosterone levels of both groups remained substantially elevated ($P < 0.01$) over those of nonstressed controls, 2 ± 1 μg/dl and were similar to those recently reported (*24*).

Foy *et al.* (*11*) reported that LTP was virtually abolished in rats exposed to 30, 1-s inescapable shocks in 30 min. By the seventh day of training, rats in the present experiment had been exposed to 30 shocks of approximately similar intensity and duration. The impairment of LTP in the yoked controls is consistent with the previous findings and indicates, furthermore, that repeated exposure to the aversive event did not result in habituation. Failure to habituate is also apparent in the continued elevation of plasma corticosterone. The most significant finding of this study, however, is that animals that could control the shock retained the ability (albeit somewhat reduced) to show LTP.

The fundamental evidence linking LTP to memory processes is its correlation with learning (*13–17*). Weisz *et al.* (*13*) reported an increase in synaptic efficacy of the dentate-granule cells during classical conditioning, and Berger (*14*) showed that potentiating the perforant path before training resulted in increased learning rates. Morris *et al.* (*15*) reported that administration of an *N*-methyl-D-asparate (NMDA) receptor antagonist (that blocks LTP) impaired learning of a spatial task, and Ott *et al.* (*16*) reported that tetanization of the perforant path as a conditioned stimulus improved avoidance behavior in the shuttle box. In contrast, Barnes and McNaughton (*17*) reported that

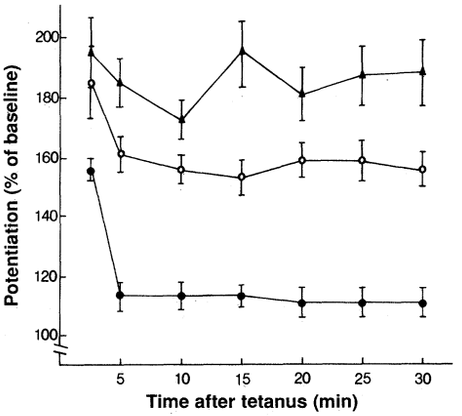

Fig. 3. Mean (± SEM) LTP of groups exposed to escapable shock (○) ($n = 12$), yoked inescapable shock (●) ($n = 12$), or no shock (▲) ($n = 12$) is expressed as the percent increase in amplitude of the pretetanus population spike from tetanus to 30 min.

tetanization of the perforant path disrupted the subsequent learning of a spatial memory task, although prior learning was not disrupted.

In our study, LTP was impaired in animals that were subjected to inescapable shock and this impairment was partially reversed by the availability of control. Although arousal level and behavioral learning may have been confounded, it is tempting to speculate that some of the learning deficits observed as a consequence of inescapable shock (*8*) were a result of impaired hippocampal LTP.

The biological substrates that govern the interaction between stress and LTP have yet to be resolved. In the initial experiment, which involved the effect of uncontrollable stress on LTP (*11*), a significant negative correlation was reported between levels of the stress-related hormone corticosterone and LTP. Subsequent experiments, however, have indicated that corticosterone is not an essential component of stress-induced LTP suppression. Adrenalectomy was reported to impair LTP (*25*), yet adrenalectomized animals exposed to inescapable shock exhibited further suppression (*26*). In our study, both groups exposed to shock displayed similar elevated corticosterone, although they differed markedly in their degree of potentiation. More likely substrates include opioid and catecholamine systems. Both are differentially altered by exposure to inescapable versus escapable shock (*1, 7*), and both modify hippocampal cell excitability (*27*).

There are at least two implications of this study. First, it indicates that controllability affects neural plasticity in the hippocampus at the cellular-synaptic level. Thus, the impairment of LTP after exposure to shock is

chiefly a consequence of "psychological" factors (that is, lack of control) rather than a consequence of the shock itself. Second, it demonstrates a behavioral manipulation that both impairs learning and modulates the induction of LTP, thereby providing further evidence that LTP may be involved in behavioral learning processes.

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Seasonal Microhabitat Selection by an Endoparasitoid Through Adaptive Modification of Host Behavior

JACQUES BRODEUR AND JEREMY N. MCNEIL*

Differences in the distribution of parasitized and unparasitized hosts has been used to infer modification of host behavior by insect parasitoids. Data are presented showing that not only do parasitized hosts behave differently from unparasitized ones, but that the behavior of parasitized hosts varies in function of the physiological state of the parasitoid. Aphids containing nondiapausing parasitoids leave the aphid colony and mummify on the upper surface of the leaves, whereas those containing diapausing parasitoids leave the host plant and mummify in concealed sites. Modification of host behavior by diapausing parasitoids results in the selection of a suitable microhabitat that reduces the incidence of hyperparasitism and should decrease the action of adverse climatic conditions during the lengthy dormant period.

THERE IS CONSIDERABLE EVIDENCE that true parasites can modify the behavior of their intermediate host, thereby increasing the probability of transmission to their final host (*1*). In the case of insects, parasitoid modification of host behavior has been inferred on the basis of differences in the distribution of parasitized and nonparasitized hosts within a habitat (*2*). However, these distributions may be unrelated to modified host behavior and instead reflect patterns of parasitoid foraging behavior (*3*). The mechanisms and adaptive significance of induced behavioral modification have received little attention, even though the ability to modify host behavior has been considered as an important aspect involved in the process of successful parasitism by parasitoids (*4*). The parasitic wasp *Aphidius nigripes* (Hymenoptera: Aphidiidae), an endoparasitoid of the potato aphid *Macrosiphum euphorbiae* (Homoptera: Aphididae), completes pupal development and facultative prepupal diapause within the mummified host. We hypothesized that if there is a selection of a suitable mummification habitat by endoparasitoid larvae under these distinctive developmental conditions, it could only occur through the modification of host behavior.

In the laboratory we noted that the position of nonparasitized aphids on potato plants differ from that of nondiapausing *A. nigripes* mummies. Detailed observation of the distribution of aphids throughout their lives showed that, under greenhouse conditions, unparasitized aphids ($n = 25$) generally remained on the undersurface of leaves [the preferred feeding area (*5*)], whereas parasitized ones ($n = 51$) often moved to the upper surface 24 to 36 hours before death (Fig. 1). This strongly supports the hypothesis that *A. nigripes* has the ability to modify host behavior before the host mummifies. However, the principal objective of our study was to examine the possibility of differential modified host behavior by nondiapausing or diapausing parasitoids, as preliminary observations suggested that the distribution of dark brown, diapausing *A. nigripes* mummies differed from that of light brown, nondiapausing ones. Experiments were therefore designed to test this

Département de biologie, Université Laval, Sainte-Foy, Québec, Canada, G1K 7P4.

*To whom correspondence should be addressed.