researchers in Europe have concluded that bovine leukemia, and therefore BLV, is transmitted via milk (*15, 16*). However, owing to the experimental design and methodology used, the data on which this conclusion was based do not indicate whether the calves became infected prenatally, by milk ingestion, or by contact. Studies conducted under appropriate experimental conditions have shown that milk-borne transmission of BLV, as compared with contact transmission, is rare if it occurs at all (*17, 18*). The resistance of calves to milk-borne infection with BLV is probably due mainly to the maternal virus–neutralizing antibodies that all calves nursed on BLV-positive dams acquire through colostrum (*17–19*).

The present study and the data on the prevalence of BLV infection in dairy herds indicate that humans are often orally exposed to BLV. Although the infectivity of BLV is apparently destroyed by pasteurization (*20*), people in many countries consume unpasteurized milk. Moreover, it is not known whether pasteurization destroys the biological activity of the proviral BLV DNA in the infected cells of milk. There is no evidence that BLV can infect humans, but neither do the data exclude this possibility. Although attempts to demonstrate BLV antibodies, particles, and antigens in humans have been negative (*1*), the findings are not conclusive because of the limited sensitivity of the assays used and because some BLV-infected cells do not synthesize virus particles or viral antigens (*2–4, 10, 11*). Molecular hybridization studies have failed to demonstrate BLV-related sequences in human tumors (*21*), but only a few tumors were examined and the probe used was only partially representative of the viral genome. While earlier epidemiological surveys showed no association between human and bovine leukemia (*1*), the most recent survey, involving a large number of cases, showed a statistically significant increase in human acute lymphoid leukemia in areas with a high incidence of bovine leukemia and BLV infection (*22*). Clearly, the question of whether BLV poses a public health hazard deserves thorough investigation with the most sensitive virological and immunological techniques available, particularly highly representative molecular probes.

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Emergence of Posttetanic Potentiation as a Distinct Phase in the Differentation of an Identified Synapse in *Aplysia*

Abstract. *The developmental time course of posttetanic potentiation was studied at an identified chemical synapse. In stage 11 juveniles (3 weeks after metamorphosis), the synaptic connections made by cholinergic neuron L_{10} onto postsynaptic neurons L_2 to L_6 were present but showed no posttetanic potentiation. In stage 13 adults (12 weeks after metamorphosis), the same tetanus resulted in an increase of 300 percent in the synaptic potential. A similar pattern was observed at two other identified synapses in the abdominal ganglion. Thus, the initial steps in synapse formation do not include the expression of this plastic capability. Rather, at least 10 weeks is required between the onset of synaptic function and the final expression of mature synaptic properties.*

Many chemical synapses in the adult animal can be altered for long periods as a result of previous stimulation. It is important in the study of neural differentiation to determine whether the capability for plastic change is part of the machinery that is present in the initial establishment of a functioning synapse, or whether these capabilities represent separate regulatory processes that emerge independently later in development.

Although the initial development and maintenance of synapses have been studied extensively (*1–4*), little is known about how neurons acquire plastic capabilities. Knowledge about the development of synaptic plasticity may help to elucidate the mechanisms of normal behavioral maturation, as well as the mechanisms that contribute to disorders in perception and motor coordination that occur when animals are reared in abnormal perceptual or motor environments (*5*). We examined posttetanic potentiation (PTP), a common form of plasticity, at an identified chemical synapse in the abdominal ganglion of the marine mollusk *Aplysia californica*. We found that PTP develops as a late step in the maturation of the synapse and is independent of transmission. The gradual emergence of PTP at an identifiable synapse provides an opportunity for studying the detailed mechanisms underlying this form of synaptic plasticity.

We used laboratory-reared animals at various stages of development, from stage 11 juveniles weighing 3 mg at 3 weeks after metamorphosis to reproductively mature, stage 13 adults weighing 100 g or more at 12 weeks after metamorphosis (*6*). We examined a specific, identified inhibitory synapse between presynaptic neuron L_{10} and one of its five identified follower cells (L_2 to L_6) located in the rostral quadrant of the left abdominal ganglion (*7*). Even in the youngest animals studied, both the pre- and postsynaptic neurons were clearly identifiable and large enough (15 μm in diameter in animals weighing 3 mg) to permit successful intracellular recordings. To obtain reliable postsynaptic potentials, we hyperpolarized the follower cells to at least 50 mV below the reversal potential of the inhibitory postsynaptic

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potential. The amount of PTP was expressed as the maximum posttetanus postsynaptic potential divided by the average pretetanus postsynaptic potential (×100).

When L_{10} is stimulated intracellularly at a rate of once every 5 seconds, or slower, the amplitude of the postsynaptic potential is fairly constant. In stage 11 juveniles weighing 3 to 15 mg (3 to 4 weeks after metamorphosis), the postsynaptic potential had a mean ± standard deviation of 13.5 ± 7.7 mV (N = 7); in stage 12 animals weighing 25 to 90 mg (5 to 12 weeks after metamorphosis), the value was 13.0 ± 1.6 mV (N = 7); and in reproductively mature, stage 13 adults weighing 100 g (more than 12 weeks after metamorphosis), it was 3.1 ± 2.7 mV (N = 4) (Fig. 1A). Despite the decrease in the amplitude of the postsynaptic potential, the actual synaptic current appears to increase steadily throughout this period of development. The input resistance of the cell decreases about 40-fold during this period, from 270 ± 60 to 7.2 ± 3.3 ohms. When this change in input resistance is taken into account, the changes in the amplitude of the postsynaptic potential suggest that the synaptic current increases about 12-fold with development (*8*).

In adult *Aplysia* weighing 100 g or more (Fig. 1B), tetanization of L_{10} at two pulses per second for 1 minute leads to a potentiation of 278 percent (the postsynaptic potential increases from 6.1 to 17 mV). With stimulation frequencies of one to ten pulses per second, the degree of potentiation is essentially independent of the rate of stimulation, provided the tetanus includes at least 100 spikes. Thus tetanization at five pulses per second for 30 seconds produced PTP that was indistinguishable from that obtained with tetanization of two pulses per second for 1 minute. When similar tetanizations were applied to animals weighing 3 to 15 mg, no potentiation was observed in any of the seven animals that were examined in this size range (Figs. 1B and 2). Even prolonged tetanization of two pulses per second for 75 seconds produced no facilitation. It is possible that a limited capacity for potentiation would be revealed with a more extreme pattern of stimulation.

Once present, PTP only gradually reaches its maximum strength with further development (Fig. 2). Stage 12 juvenile animals weighing 1.4 to 2.1 g showed PTP of 210 ± 48 percent (N = 3), whereas reproductively mature, stage 13 adults weighing 40 to 100 g showed PTP of 279 ± 63 percent (N = 6). In contrast to the gradual development of the magnitude of PTP, the decay time of PTP (once PTP was present) was almost constant throughout development (45 ± 7 seconds, N = 22). This constancy in the decay of PTP suggests that the basic kinetics for the potentiation are determined as soon as PTP can first be detected, and that subsequent changes in the amount of PTP probably reflect quantitative changes in PTP with later growth and development.

The failure to detect PTP in very young animals could result from a ceiling effect (*7*). The postsynaptic potential in very young animals (13.5 ± 7.7 mV; N = 7) is large before tetanization, perhaps too large to show further potentia-

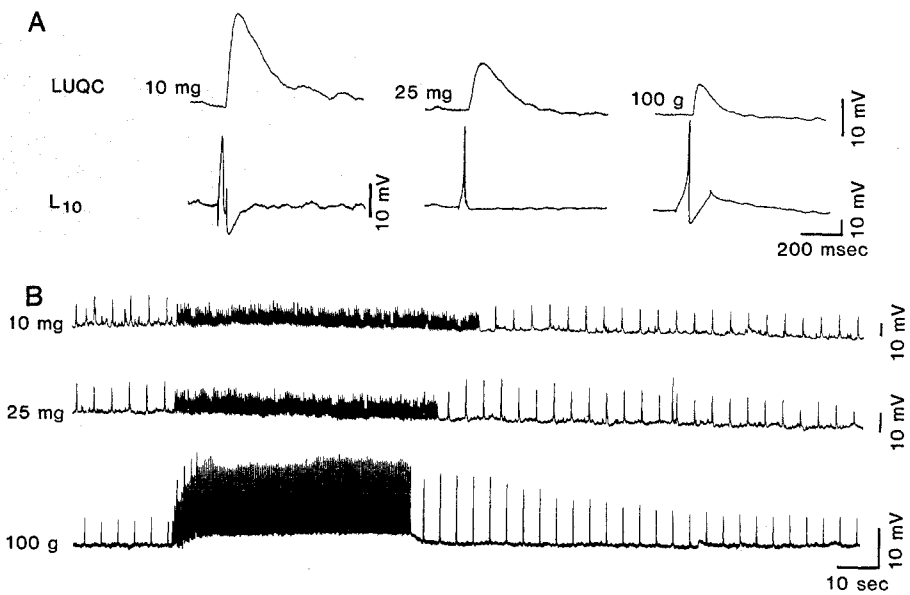

Fig. 1. (A) Synaptic transmission from the identified interneuron L_{10} to left-upper-quadrant follower cells (*LUQC*) in the final three stages of *Aplysia* development. Spikes in L_{10} evoke inhibitory postsynaptic potentials in LUQC, which appear inverted here as a result of hyperpolarization of the follower cells to about 50 mV below the inhibitory postsynaptic reversal potential (in order to obtain large, reliable postsynaptic potentials). Despite a probable large increase in synaptic transmitter release between stages 11 and 13, the amplitude of the postsynaptic potential actually decreases with development because of a concomitant profound drop in cell input resistance. (B) Developmental change in PTP examined in the same animals as in (A). The control and the test postsynaptic potentials were evoked with 0.2-Hz stimulation of L_{10}. In the stage 11 animal (10 mg), L_{10} was tetanized for 66 seconds at 2 Hz, producing PTP of 148 percent. The input impedance of the follower cell was 100 ohms, and the diameter was 30 μm. In the stage 13 animal (100 g), L_{10} was tetanized for 60 seconds at 2 Hz, producing PTP of 278 percent. The input impedance of the follower cell was 6.3 ohms, and the diameter was 500 μm.

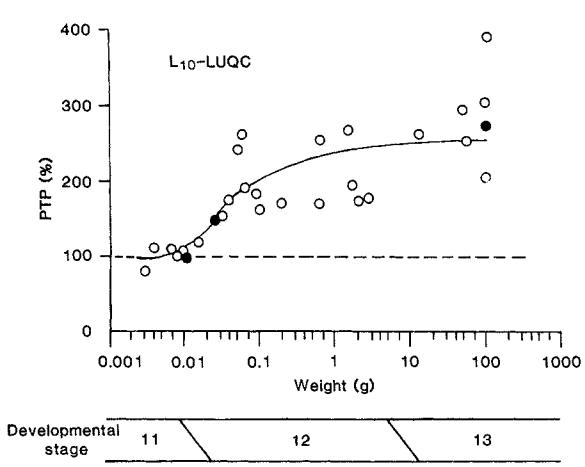

Fig. 2. Magnitude of PTP as a function of age, measured by animal weight. The closed circles correspond to the animals presented in Fig. 1. The curve was fitted by eye. Since there is a strong correlation (regression coefficient, .93) between animal weight and the diameters of the identified neurons L_{10}, R_{15}, and the inhibitory follower cells of L_{10}, we have used animal weight as a measure of age in order to obtain a better resolution than that obtained by the established staging criteria that refer to external markings and describe fairly sizable periods of the animal's growth (*5*). Stage 11, the appearance of rhinophores, corresponds to animals weighing less than 10 mg; stage 12, the appearance of the genital groove, corresponds to weights between 10 mg and 10 g; and stage 13, reproductive maturity, corresponds roughly to animals weighing more than 10 g. During development, PTP appears late in stage 11 and takes until late in stage 12 to reach the magnitude seen in the adult.

tion after tetanus. Although the follower cell was significantly hyperpolarized (sometimes as much as 60 mV below the reversal potential of the inhibitory postsynaptic potential), it is possible that the postsynaptic potential approached its reversal potential sufficiently closely that a ceiling effect might have prevented a clear demonstration of facilitation. We therefore reduced the transmitter output of the presynaptic neuron by hyperpolarizing the presynaptic cell. The amount of transmitter released by L_{10} is directly related to presynaptic membrane potential (*9*). Thus, in a juvenile animal weighing 6 mg, hyperpolarizing L_{10} by 5 mV reduced the postsynaptic potential from 10.3 to 7.3 mV. Despite this, the amount of PTP was essentially unchanged (95 percent with presynaptic hyperpolarization compared to 104 percent without). To rule out a ceiling effect further, we compared two groups of animals at different stages of development where the control postsynaptic potential was almost the same. In stage 11 animals, PTP was nonexistent (102 ± 12 percent; $N = 7$) with a postsynaptic potential of 13.5 ± 7.7 mV, whereas in stage 12 animals, PTP was clearly present (193 ± 42 percent, $N = 7$) with a postsynaptic potential of 13.0 ± 1.6 mV. These results suggest that PTP appears at a late stage in development, in this instance taking at least 1 month to fully develop, after a functional connection has been established (*10*).

To determine the generality of this result in *Aplysia*, we next investigated two identified excitatory synaptic connections that show robust PTP in the adult (*8*). We first examined the excitatory connections of the same presynaptic neuron L_{10} onto another class of follower cells, the RB cells, and found a trend almost identical to that for the inhibitory synapses. In a few instances, we examined both inhibitory and excitatory connections in the same ganglion and found equivalent PTP at both synapses. (In a 1.7-g animal, the PTP was 192 percent for the inhibitory and 206 percent for the excitatory postsynaptic potential; these values were 260 and 262 percent in a 12-g animal and 247 and 247 percent in a 60-g animal.) This experiment independently supports the now well-established idea that PTP is a purely presynaptic process resulting from enhanced mobilization of transmitter (*11*). We observed a similar time course for the emergence of PTP at the identified excitatory synapse made by an axon within the right connective onto identified neuron R_{15} (RC_1 to R_{15}) (*12, 13*) in a similarly detailed study. In each case, the emergence of PTP occurred long after the initial chemical synaptic connections had been established. The finding that synapses involving different presynaptic neurons and different postsynaptic cells show a similar time of onset of PTP suggests that PTP may be induced synchronously throughout a particular neural region at a specific time during development.

The late appearance of PTP during development suggests that the capability for this form of synaptic plasticity is an independent regulatory process that is superimposed upon the basic mechanisms of synaptic transmission. The absence of PTP early in development and its gradual emergence after metamorphosis provide a potentially useful experimental system for elucidating the molecular mechanisms underlying PTP. The appearance of PTP should correlate in time with the appearance of the missing component.

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Demineralization of Porous Solids

Abstract. *When a porous ionic solid is placed in acid, the acid will dissolve surface material. When this dissolved material and the acid diffuse into the solid's pores, they can precipitate more solid. If the acid is buffered, the diffusing species can bring about precipitation in some regions and dissolution in others. When the porous solid contains several chemical species, the diffusion can precipitate one species and dissolve another. The results have implications for the demineralization of teeth.*

This work explores how diffusion and chemical reaction affect the dissolution by acid of porous ionic solids. How this dissolution proceeds depends on the relative speed of diffusion and reaction. When the bulk of the solution next to the solid is rapidly stirred, the acid can diffuse to the solid's surface very quickly and react with it. If the solid is essentially impermeable, containing a very few pores, then any ions produced by the dissolution are quickly swept back into the bulk solution. Because diffusion and chemical reaction occur sequentially, the overall dissolution rate depends on the sum of the resistances of diffusion and reaction. Such a process represents an important limit of corrosion, and it is this limit that is usually studied (*1*).

Alternatively, the solution next to the solid may not be well stirred and the solid may be highly porous (Fig. 1). In this case, the acid concentration will drop as it approaches the solid's surface and continue to drop within the solid's pores. The ions produced as a result of the acid-solid reaction will be present in the highest concentration near the surface. From this maximum, they can diffuse out into the bulk solution or further into the porous solid. Within the solid diffusion and reaction occur simultaneously, so that the overall dissolution rate is no longer a simple sum of the resistances of diffusion and reaction.

To calculate this dissolution rate, we assume that all chemical reactions in the solid are much faster than the diffusion

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