measurements in humans [C. E. Ferree and G. Rand, in *Report of a Joint Discussion of Vision*, A. O. Rankine and A. Ferguson, chairmen (Physical Society, London, 1942), pp. 244–262.

7. The fact that we scored only photographs that were on-axis sometimes resulted in missing data points. We always photographed with at least three target distances for each infant (typically 0.25, 0.5, and 1.0 m or 0.5, 1.0, and 2.0 m). However, missing data points sometimes resulted in accommodative functions being derived from only two target distances (see Fig. 1). For some animals at some target distances, we obtained more than one photograph that could be scored. These repeated measures provide an estimate of the reliability of our method. Standard deviations calculated from these repeated measures were typically about 0.25 diopter and ranged from 0.10 to 0.67 diopter.
8. When the animal is focused hyperopically relative to the camera, the distal tips of the orthogonal star arms are reddish in hue; when myopically focused, the tips are blue. The effect is due to the longitudinal chromatic aberration of the eye, and is particularly apparent in simian eyes.
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Long-Term Synaptic Potentiation in the Superior Cervical Ganglion

Abstract. *Brief tetanic stimulation of the preganglionic nerves to the superior cervical ganglion enhances the postganglionic response to single preganglionic stimuli for 1 to 3 hours. This long-term potentiation of transmission through the ganglion is apparently not attributable to a persistent muscarinic action of the preganglionic neurotransmitter, acetylcholine, since neither the magnitude nor the time course of the phenomenon is reduced by atropine. The decay of long-term potentiation can be described by a first-order kinetic process with a mean time constant of 80 minutes. We conclude that long-term potentiation, once considered a unique property of the hippocampus, is in fact a more general feature of synaptic function. This form of synaptic memory may significantly influence information processing and control in other regions of the nervous system, including autonomic ganglia.*

Long-term potentiation (LTP), a use-dependent form of enhanced synaptic efficacy, can last for hours, days, or even weeks (*1, 2*). It can be induced by tetanic activation of the synapses for only a few seconds. Partly for these reasons, LTP has been considered by many to provide a possible neuronal substrate for certain aspects of learning and memory (*1, 3, 4*). The only published reports of LTP have been in studies of the hippocampus, a brain region long implicated in learning and memory functions (*4, 5*). It is therefore natural to ask whether LTP is an exclusive property of hippocampal synapses or a more general feature of neuronal function. We have investigated the superior cervical sympathetic ganglion, a peripheral nervous system structure not traditionally associated with learning and memory (*6–8*). We have found LTP in the sympathetic ganglion and describe it by a first-order kinetic process.

The ganglion was removed (from decapitated Sprague-Dawley rats), decapsulated, and maintained at room temperature in oxygenated Locke solution (*9*). Supramaximal stimuli were applied to the preganglionic (cervical sympathetic) nerve via a suction electrode coupled to an isolated stimulator (Fig. 1A) (*10*). Records of compound action and synaptic potentials were recorded by a suction electrode applied to the internal carotid (postganglionic) pole of the ganglion, the signal from which was differentially amplified (2 Hz to 10 kHz) and displayed for photography on a storage oscilloscope. In some experiments, the responses were digitized and stored by computer for later analysis. Sometimes a loop of the preganglionic nerve was sucked into a second recording electrode, and the response from this electrode was similarly amplified and displayed on a second trace of the oscilloscope (Fig. 1A). Thus, preganglionic stimulation set up a volley of action potentials conducted past one recording electrode into the body of the ganglion to excite synaptically postganglionic neurons whose response was recorded with a second suction electrode. Normally, supramaximal stimulation of the preganglionic nerve was sufficient to initiate action potentials in nearly all of the postganglionic neurons. In order to spare postganglionic neurons for recruitment during an increase in synaptic efficacy, we reduced synaptic excitation either by adding curare (100 to 150 μM) or by suitable changes in the Ca^{2+} and Mg^{2+} concentrations (*11*) in the bathing medium. In most of the experiments reported here, atropine (2 μM) was added to the Locke solution to block muscarinic responses (*7, 12*). The amplitudes of postganglionic responses to single preganglionic stimuli were measured at 1-minute intervals for 5 to 60 minutes before and 1 to 3 hours after tetanic preganglionic stimulation (20 Hz for 10 to 20 seconds).

During the tetanic preganglionic stimulation, the amplitude of the postganglionic response rapidly decreased because of synaptic depression. However, a single preganglionic stimulus delivered 1 minute after the tetanus produced a postganglionic response that was more than twice as large as control responses measured before the tetanus. Subsequently, the postganglionic response progressively decreased in amplitude, but it remained elevated above control (pretetanic) levels for more than an hour after the tetanus (Fig. 1B, inset). This was a highly reproducible observation in the more than 20 ganglia studied.

To evaluate the decay kinetics of the enhanced synaptic transmission, we transformed the voltage-amplitude data into a dimensionless incremental response $I(t)$ that normalized the posttetanic response amplitude to a fractional increase over the pretetanic control response amplitude

$$I(t) = [V(t) - V_C]/V_C \quad (1)$$

where V_C is the mean control value and $V(t)$ is the posttetanic value as a function of time t (*8, 13*). A semilogarithmic plot of the time course of $I(t)$ showed that there was always an early rapid decay phase followed by a much more slowly decaying phase (Fig. 1B). The simplest expression that we found to describe accurately the overall posttetanic time course of the enhanced response consisted of the sum of two exponential terms

$$I(t) = P\exp(-t/\tau_P) + L\exp(-t/\tau_L) \quad (2)$$

where P is the early, rapidly decaying component and L is the slowly decaying, long-term component. The magnitudes (P and L) and time constants (τ_P and τ_L) of these components were determined by standard exponential fitting and peeling (*14*). That we could accurately describe the entire posttetanic time course in terms of Eq. 2 (Fig. 1B) suggests the possibility of two first-order kinetic processes. For convenience, and by analogy to similar phenomena observed by other investigators, we refer to the more rapidly decaying component as posttetanic potentiation (PTP) and the slowly decaying component as LTP (*15*).

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Table 1. Descriptive parameters for the characteristics of enhanced posttetanic synaptic transmission in the ganglion (*14, 15*).

Parameter	Mean ± standard error	Range	*N*
PTP magnitude (*P*)	1.0 ± 0.2	0.2 to 2.0	10
PTP time constant (τ_P) (minutes)	3.2 ± 0.5	1.2 to 5.8	10
LTP magnitude (*L*)	1.2 ± 0.2	0.7 to 2.9	10
LTP time constant (τ_L) (minutes)	82 ± 26	34 to 230	10
Magnitude ratio* (*L*/*P*)	1.8 ± 0.4	0.4 to 4.5	10
Time constant ratio*(τ_L/τ_P)	29 ± 5	12 to 60	10

*The mean of a ratio between two variables is not necessarily equal to the ratio of their mean values.

In Fig. 1B, curve 2 is from a ganglion that showed the largest value of τ_L we have observed (230 minutes), and curve 4 is from a ganglion with the smallest value of τ_L we have seen (34 minutes). The results of similar analyses done in ten ganglia (all bathed in 2 μM atropine) are summarized in Table 1. To evaluate the statistical independence for the four parameters—*P*, τ_P, *L*, and τ_L—the six possible correlations among these parameters were calculated. None of the correlations approached statistical significance.

Neither component of the posttetanic increase in response seemed to be due to recruitment of additional afferents in the preganglionic nerve. We always used supramaximal stimulation, and the presynaptic volley amplitude never showed a posttetanic increase and sometimes showed a transient decrease. The occurrence of LTP did not depend on the presence of curare in the bath. When curare was eliminated and the Ca^{2+} and Mg^{2+} concentrations were adjusted (*11*) to produce submaximal responses, LTP could still be induced. In another series of experiments, we tetanically stimulated the postganglionic axons with the same stimulus parameters previously used to induce LTP by excitation of the preganglionic fibers. This postganglionic excitation was not sufficient to induce LTP when tested by subsequent preganglionic stimulation.

Two considerations suggest that the LTP was not due to the persistence of muscarinic responses of the kind first reported by Volle (*16*) or more recently by Libet (*17*). (i) The concentrations of atropine (2 μM) we used should have blocked all muscarinic responses in these cells (*7, 12*). (ii) In successive trials on the same ganglion, the magnitude and duration of LTP induced in the presence of atropine were as large or larger than those induced in the absence of atropine.

We found that PTP decayed with the same time constant (about 3 minutes) reported previously for PTP in rabbit ganglia at 22°C (*8*). By contrast, the LTP observed decayed with a mean time constant of about 80 minutes, and it therefore lasted for hours (*19*). These results suggest that if one wishes to investigate LTP uncontaminated by PTP, one should wait at least 10 minutes (three

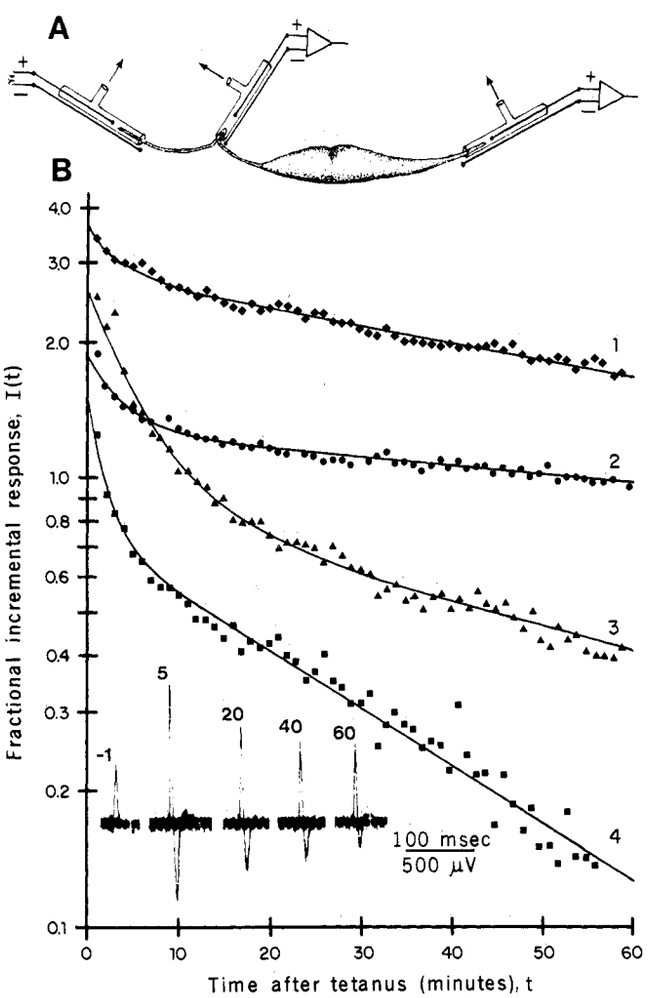

Fig. 1. (A) Typical stimulating and recording arrangement. The internal carotid nerve (right) is in a recording suction electrode, and the preganglionic nerve (left) is in the stimulating suction electrode. The arrows indicate direction of suction applied to the stimulating or recording electrode. (B) Time course of the decay of posttetanic enhanced transmission after 10 to 20 seconds of 20-Hz stimulation. The four plots represent data from different ganglia, and the solid lines are the curves computed from Eq. 2. For convenience, data points taken at times longer than 60 minutes are not illustrated. In general, we discontinued the data analysis when the responses declined to about 10 percent above control levels [$I(t) = 0.1$] because of the increased coefficient of variation. (Compare the variability in the data points associated with curves 1 and 4 at $t = 50$ min.) Inset: Representative postganglionic recordings taken from curve 3 at the times (in minutes, relative to the end of tetanic stimulation) indicated.

times τ_P) after tetanus, at which time the PTP component should have become negligible.

We conclude that LTP is present in the sympathetic ganglion and is thus not a unique property of hippocampal synapses. The unique feature of LTP is the long duration of increased synaptic efficacy (hours) after brief (seconds) stimulation. Although this aspect of LTP is similar in the ganglia and the hippocampus, it is not known whether the underlying mechanisms are similar. The sympathetic ganglia should provide an easily accessible preparation with which to study this phenomenon and determine its role in nervous system function. The possible normal physiological role of activity-dependent synaptic plasticity in the sympathetic ganglion has been discussed elsewhere (*19*).

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15. We have followed the convention of Magleby and co-workers (*8*, *13*) in identifying the kinetic component with a decay time constant on the order of a few minutes as PTP. We use the term LTP to refer to any increase in the efficacy of synaptic transmission that (i) can be produced by brief presynaptic tetanic stimulation (10 to 30 seconds) and (ii) is associated with a decay time constant or duration at least a decade longer than that associated with PTP (Table 1).
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Onset and Offset of Brain Events as Indices of Mental Chronometry

Abstract. *Analysis of single-trial electroencephalogram waveforms in a reaction time task demonstrated that the onset and offset values of event-related potentials can be used as indices of the duration of information processing. Two negative waves have been identified which peak at different times in different regions of the scalp, with the second overlapping the last part of the first. These waves are related in different ways to the duration of perceptual processing.*

Mental chronometry in humans is an important issue in cognitive psychology (*1*). Progress in its understanding has been made through electroencephalogram (EEG) studies, particularly those concerning the endogenous P300 or P3 wave (*2*). However, the P300 is preceded by a negative wave, N200 or N2. The peak latency of both waves was reported to covary with perceptual processing (*2–4*).

We report the existence of two types of N200 waves, which are related in different ways to the same behavioral response; the duration of one increases with reaction time, and that of the other remains constant. These results provide clues to the different functions of the waves and may help in the conceptualization of information processing in humans.

The N200 wave can be isolated for observation by removing the overlapping sensory P2 component; this can be accomplished by omitting an expected stimulus and rendering the omission relevant for the subject. However, even after the occurrence of a relevant stimulus, N200 can be isolated by subtracting the evoked potential obtained in a passive situation (*5–7*). Both subtraction and omission studies have shown that N200 may be a better index than P300 of the temporal course of information processing related to stimulus evaluation and sensory-motor decision. In contrast to P300, which sometimes peaks after the behavioral response, N200 always precedes the response (*3*, *4*). Furthermore, unlike the P300, the distribution of N200 on the scalp varies with stimulus modality (*6*, *8*, *9*).

Two types of N200 have been described for the visual modality: one is central and the other parieto-occipital. They were observed in both reaction time and counting tasks and therefore cannot be attributed to the movement-

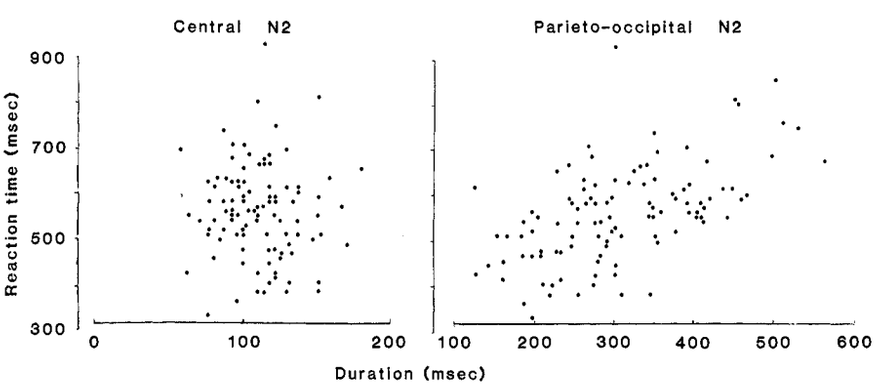

Fig. 1. Duration of Cz:N265 (left) and of POz:N220 (right) as a function of the reaction time of seven subjects during 107 trials.

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