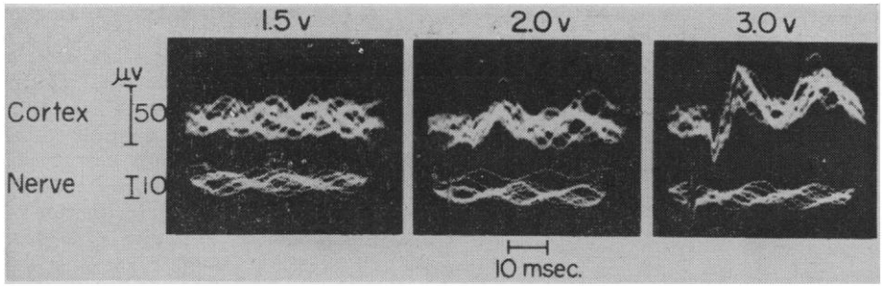

Fig. 1. Superficial radial nerve and cortical responses to varying intensities of stimulation (stimulus duration, 0.01 msec). Ten superimposed sweeps in each. At 1.5 volts only the stimulus artifact is recorded; at 2.0 volts a barely detectable response appears in the nerve while the cortical response is quite apparent; at 3.0 volts both responses are clear.

sponses were amplified by Tektronix type 122 preamplifiers, displayed on a Tektronix type 502 dual beam oscilloscope, and photographed with a Dumont Polaroid camera.

Four animals were studied in the unanesthetized state, after they had been prepared surgically under ether and then immobilized with gallamine triethiodide (Flaxedil) and placed under artificial respiration. The remaining animals were studied under light-to-moderate pentobarbital anesthesia. Cortical records were obtained from somatosensory areas I and II by means of monopolar wick or silver–silver chloride balls with the indifferent electrode on the cut edge of the scalp; depth electrodes were bipolar nichrome wires insulated except at the tips; nerve recordings were from either stainless steel bipolar needles inserted through the nerve or bipolar silver plates on which the nerve rested.

In all instances, stimuli capable of evoking responses either subcortically or in the peripheral nerve also elicited responses from the cortex. Figure 1 illustrates responses elicited by varying intensities of nerve stimulation in simultaneous recordings from superficial radial nerve and somatosensory I in an unanesthetized cat. It can be seen that when stimulation results in peripheral responses, responses are also evoked in the cortex. Identical results were obtained in all animals, anesthetized and unanesthetized. These results are in accord with those of Mark and Steiner (*5*) on deeply anesthetized cats.

The data of Shagass and Schwartz (*2*) indicate that a necessary, though not sufficient, condition for the occurrence of human perception is the elicitation of responses at the cortex. Obviously responses cannot be elicited from the cortex by a stimulus which has not excited the peripheral nerve. Present results and those of Dawson (*4*) indicate, however, that there are no responses peripherally or subcortically without the concurrent evocation of responses in the cortex.

In view of these results, it would appear that the term "*subliminal perception*" is a misnomer in regard to those experiments in which stimuli below threshold for perception are applied (for example, *6*). If these stimuli are truly subliminal, perception *cannot* occur. They have no effect on the nervous system. Those experiments on "subliminal" perception which do employ stimuli capable of producing nervous system responses would seem to be dealing mainly with the relationship between perception and attention. These stimuli may or may not be immediately perceived, depending upon factors, such as distraction, which influence "focus of attention." The experiments of Hernández-Peón *et al.* (*7*) demonstrate a neurophysiological correlate of fluctuations of perception under different conditions of attentiveness. In these experiments evoked sensory potentials diminished when a different and more attention-getting stimulus was concurrently introduced. However, it should be clearly recognized that, although no longer attended to, these stimuli were not subliminal (*8*).

MARVIN SCHWARTZ
CHARLES SHAGASS
Department of Psychiatry, Psychopathic Hospital, State University of Iowa, Iowa City

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Cellular Adaptation to Morphine in Rats

Abstract. The respiration of KCl-stimulated cortical slices of brain from control rats is markedly depressed by morphine, whereas the respiration of those from rats chronically dosed with morphine is unaffected. The results demonstrate an adaptation to morphine at the cellular level which is concomitant with the adaptation of the whole animal to morphine.

The stimulatory effect of 0.1*M* potassium chloride on the oxidation of cortical slices from the brain in the presence of glucose is well established. Since the original observation of this effect by Ashford and Dixon (*1*), several workers have studied the effect of depressant agents such as various barbiturates (*2, 3*), hypnotics (*2, 3*), and ethanol (*3, 4*) on the oxidation of KCl-stimulated cortical slices. These authors found a marked depression of the oxidation of stimulated slices with depressant agents at concentrations which are relatively ineffectual, or even stimulatory in the case of ethanol, on the oxidation of unstimulated slices. Studies were never made on cortical slices of brain obtained from an animal chronically treated with depressant agents.

Male Holtzman rats, weighing 200 to 300 g, were chronically morphinized intraperitoneally with an initial dose of 15 mg/kg twice daily, which was increased in 15-mg/kg increments weekly

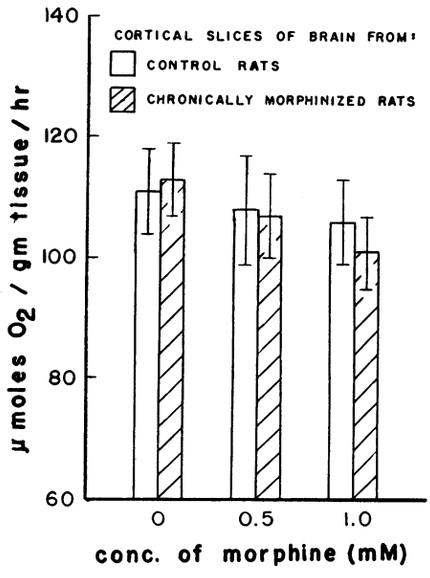

Fig. 1. Effect of morphine on the oxidation of unstimulated cortical slices. Each bar represents an average of 15 rats. The vertical lines at the top of each bar show the standard error. None of the groups are significantly different ($p > 0.2$) from their respective control groups (no morphine).

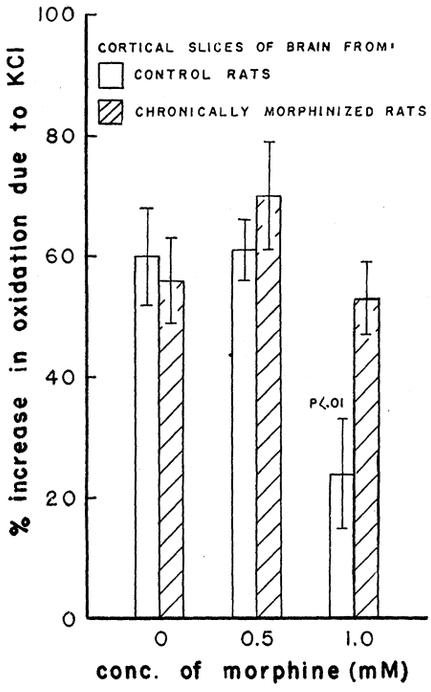

Fig. 2. Effect of morphine on the stimulated oxidation of cortical slices. Each bar represents an average of 15 rats. The vertical lines at the top of each bar show the standard error. Only one group, as indicated ($p < 0.01$), is significantly different from the control group (no morphine).

for 3 weeks until the rats were receiving 45 mg/kg twice daily during the third week. The rats became tolerant to the depressant and analgesic effects of morphine during this treatment. Control animals received isotonic saline injections throughout the course of the experiment. Eighteen hours after the last dose, the rats were decapitated and cortical slices of their brains were prepared for analysis.

Respiration was measured manometrically by the conventional Warburg technique at 37°C with oxygen as the gas phase. The incubating medium contained 0.135*M* NaCl, 0.005*M* KCl, 0.0013*M* $MgSO_4$, 0.0005*M* $CaCl_2$, 0.012*M* glucose, and 0.01*M* KH_2PO_4–Na_2HPO_4 buffer, *p*H 7.4. After readings were taken every 10 minutes for 40 minutes, KCl (0.1*M*) or various concentrations of morphine or both were tipped from the side arm into the main compartment, and readings were taken for an additional 50 minutes at 10-minute intervals. There was a 10-minute lag period before the effect of KCl became fully apparent and before the rate again became linear.

At concentrations of 5×10^{-4} and 1×10^{-3} *M* morphine does not affect the oxidation of unstimulated cortical slices from control or chronically morphinized rats (Fig. 1). This agrees with other reports (*5*) that morphine is without effect at concentrations as high as $3.2 \times 10^{-3}M$ and 0.01*M*. Potassium chloride stimulates the oxidation of slices from both control and chronically morphinized rats to about 60 percent above the unstimulated rate in the absence of morphine (Fig. 2). The respiratory stimulation of slices from control rats is only about 24 percent in the presence of $1 \times 10^{-3}M$ morphine, while the respiratory stimulation of slices from morphinized rats remains unaffected. At a concentration of $5 \times 10^{-4}M$ morphine appears to have no significant effect on the stimulated slices from either control or chronically morphinized rats. The results show an adaptation to morphine at the cellular level. This adaptation occurs at a time when the whole animal is pharmacologically adapted to the effects of morphine.

Eddy (*6*) pointed out that among the numerous explanations offered for the phenomenon of tolerance to narcotic analgesics, increased biotransformation of the drug and cellular adaptation have the greatest likelihood for clarifying this problem. The metabolism of morphine in tolerant animals appears to be unrelated to the development of tolerance (*7*). In fact, enzymic studies show less *N*-demethylating capacity (*8*) and less transferase activity (*9*) in livers obtained from tolerant rats than in livers obtained from nontolerant rats. Cellular adaptation is an attractive explanation for the formation of tolerance, but supporting evidence for this hypothesis is meager.

Although the in vitro concentration of morphine employed in this study is still quite high compared to the theoretical in vivo concentration of morphine in the central nervous system, the demonstration of a definite difference between the tissues from control and chronically morphinized rats in resisting the depressive effect of morphine offers a promising tool for studying cellular adaptation in vitro (*10*).

A. E. TAKEMORI

Department of Pharmacology, State University of New York, Upstate Medical Center, Syracuse

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Stability of Protein in Intestinal Epithelial Cells

Abstract. In vivo measurements have revealed a high degree of stability of synthesized protein in rapidly proliferating intestinal epithelial cells. A slow loss of protein has been found during migration of mature cells to the villus tip.

Although previous studies have provided support for the concept of "dynamic equilibrium" of proteins in mammalian cells (*1*), the occurrence of rapid intracellular protein degradation and turnover has recently been questioned (*2*). In bacteria, several studies (*2, 3*) have indicated that protein, once synthesized, is stable. The rates of protein degradation here were so low that dynamic intracellular protein turnover was not believed to play a role in protein synthesis in these cells. Recently, similar evidence was found in mammalian cells of the L strain grown in tissue culture (*4*). In addition, although protein breakdown was found in resting yeast cells, a much smaller rate of degradation was present in dividing cells (*5*). The results of the present studies, performed in vivo, suggest that visceral parenchymal cells which are renewed rapidly maintain a high degree of stability of synthesized proteins with little degradation, while protein breakdown or loss is greater in the older nonproliferating cells derived therefrom.

The incorporation of labeled leucine into proteins of the jejunum was measured. Adult C57 Brown mice were maintained on a standard nutritional diet. Microautoradiographic measurements were made of the cells of the proximal jejunum removed after intraperitoneal injection of 100 μc of tritiated leucine (specific activity, 370 mc/mmole). Chromatographic analysis of injected material revealed no free label. In addition, the tissues were washed with solutions containing trichloracetic acid, and chemical analysis revealed no free amino acid present, indicating that most grains activated