3. The activities of hydroxyindole-*O*-methyltransferase and *N*-acetyltransferase, enzymes necessary for the synthesis of melatonin, are suppressed by light [R. J. Wurtman, J. Axelrod, L. S. Phillips, *Science* **142**, 1071 (1963); D. C. Klein and J. L. Weller, *ibid.* **177**, 532 (1972)].
4. C. L. Ralph, D. Mull, H. J. Lynch, L. Hedlund, *Endocrinology* **89**, 1361 (1971).
5. R. Y. Moore and N. J. Lenn, *J. Comp. Neurol.* **146**, 1 (1972).
6. J. A. Ariens Kappers, *Z. Zellforsch. Mikrosk. Anat.* **52**, 163 (1960).
7. Human melatonin secretion seems to be controlled by sympathetic neurons since propranolol blocks the nighttime secretion of melatonin [G. M. Vaughan *et al.*, *J. Clin. Endocrinol. Metab.* **42**, 752 (1976); T. Hanssen, T. Heyden, T. Sundberg, L. Wetterberg, *Lancet* **1977-II**, 309 (1977)] and since the 24-hour rhythm of secretion is absent in patients with transection of the cervical spinal cord [L. W. Kneisley, M. A. Moskowitz, H. J. Lynch, *J. Neural Transm.* **13**, 311 (1978)] and in patients with chronic autonomic failure [G. M. Vaughan, S. D. McDonald, R. M. Jordan, J. P. Allen, R. Bell, E. A. Stevens, *Psychoneuroendocrinology* **4**, 351 (1979); M. Tetsuo, R. Polinsky, S. P. Markey, I. J. Kopin, personal communication].
8. D. C. Jimerson, H. J. Lynch, R. M. Post, R. J. Wurtman, W. E. Bunney, Jr., *Life Sci.* **20**, 1501 (1977); H. J. Lynch, D. C. Jimerson, Y. Ozaki, R. M. Post, W. E. Bunney, Jr., R. J. Wurtman, *ibid.* **23**, 1557 (1978).
9. T. Akerstedt, J. E. Froberg, Y. Friberg, L. Wetterberg, *Psychoneuroendocrinology* **4**, 219 (1979).
10. J. Arendt, *J. Neural Transm.* **13** (Suppl.), 265 (1978); G. M. Vaughan, R. Bell, A. Dela Pena, *Neurosci. Lett.* **14**, 81 (1979).
11. L. Wetterberg, *J. Neural Transm.* **13** (Suppl.), 289 (1978).
12. M. J. Perlow, S. M. Reppert, L. Tamarkin, R. J. Wyatt, D. C. Klein, *Brain Res.* **182**, 211 (1980).
13. Since intense light can produce serious retinal injury in experimental animals [M. O. Tso and F. G. LaPiana, *Trans. Am. Acad. Ophthalmol. Otolaryngol.* **79**, 788 (1975); T. Kuwabara and M. Funahashi, *Arch. Ophthalmol.* **94**, 1369 (1976)], several precautions were taken to ensure our subjects' safety. Protective screens were provided to diffuse the light and reduce thermal energy. The subjects were instructed to look only briefly at the light source and not to look at it if they experienced any discomfort.
14. A. J. Lewy and S. P. Markey, *Science* **201**, 741 (1978).
15. S. M. Reppert, M. J. Perlow, L. Tamarkin, D. C. Klein, *Endocrinology* **104**, 295 (1979).
16. Exposure to 1500 lux seems to cause a biphasic rate of decline in melatonin: an initial rapid rate, similar to that caused by 2500 lux, followed by a slower rate. This pattern resembles that of the decrease in *N*-acetyltransferase and pineal melatonin in rats after exposure to fluorescent light for 1 minute [H. Illnerova, M. Backstrom, J. Saaf, L. Wetterberg, B. Vangbo, *Neurosci. Lett.* **9**, 189 (1978); H. Illnerova, J. Vanacek, J. Krecek, L. Wetterberg, J. Saaf, *J. Neurochem.* **32**, 673 (1979)].
17. We did not measure light at each discrete wavelength. Melatonin secretion in albino rats is most sensitive to blue-green light, the same wavelength (530 nm) that activates retinal rhodopsin [D. P. Cardinali, F. Larin, R. J. Wurtman, *Proc. Natl. Acad. Sci. U.S.A.* **69**, 2003 (1972)]. The action spectra for melatonin suppression in humans must still be determined.
18. K. P. Minneman, H. J. Lynch, R. J. Wurtman, *Life Sci.* **15**, 1791 (1974).
19. T. Deguchi and J. Axelrod, *Proc. Natl. Acad. Sci. U.S.A.* **69**, 2547 (1972); H. Illnerova and J. Vanacek, *Brain Res.* **167**, 431 (1979).
20. S. M. Reppert, M. J. Perlow, L. Tamarkin, D. Orloff, and D. C. Klein (personal communication) informed us that 4 hours of 15-W Cool White fluorescent light (450 lux at eye level) suppressed the level of melatonin in rhesus monkey cerebrospinal fluid; secretion resumed when the monkeys were returned to darkness during the last third of the night. Melatonin secretion in sheep is stopped by exposure to Cool White fluorescent light of 500 lux [M. D. Rollag and G. D. Niswender, *Endocrinology* **98**, 482 (1976)].
21. Some investigators did speculate that humans might require light of higher intensity (*8*, *9*); some also proposed that "extrapineal sources of melatonin" could mask an effect of light on the pineal gland (*9*, *23*). However, we demonstrated that significant amounts of melatonin could not be detected in the plasma of pinealectomized rats by GC-MS [A. J. Lewy, M. Tetsuo, S. P. Markey, F. K. Goodwin, I. J. Kopin, *J. Clin. Endocrinol. Metab.* **50**, 204 (1980)]. Our results contradicted those of H. J. Lynch, Y. Ozaki, D. Shakal, and R. J. Wurtman [*Int. J. Biometeorol.* **19**, 267 (1975)] and Y. Ozaki and H. J. Lynch [*Endocrinology* **99**, 641 (1976)], who used bioassays or radioimmunossays.
22. J. Arendt, L. Wetterberg, T. Heyden, P. C. Sizonenko, L. Paunier, *Horm. Res.* **8**, 65 (1977); E. D. Weitzman, U. Weinberg, R. D'Eletto, H. Lynch, R. J. Wurtman, C. Czeisler, S. Erhlich, *J. Neural Transm.* **13** (Suppl.), 325 (1978); U. Weinberg, R. D. D'Eletto, E. D. Weitzman, S. Erlich, C. S. Hollander, *J. Clin. Endocrinol. Metab.* **48**, 114 (1979).
23. G. M. Brown, S. N. Young, S. Gauthier, H. Tsui, L. J. Grota, *Life Sci.* **25**, 929 (1979).
24. We delayed the light-dark and activity-rest cycles of two subjects for 4 hours by having them sleep between 3 a.m. and 11 a.m. After 1 week, their nighttime secretion of melatonin began after 3 a.m. and reached its peak between 9 a.m. and 10 a.m. On the eighth day of the study the subjects were awakened at 7 a.m. (after 4 hours of sleeping in the dark) and were exposed to sunlight: the concentration of melatonin decreased 56 percent within 1 hour and was 10 pg/ml before 11 a.m.
25. J. A. Elliot, *Fed. Proc. Fed. Am. Soc. Exp. Biol.* **35**, 2339 (1976).
26. S. Timonen, B. Franzar, K. Wichmann, *Ann. Chir. Gynaecol. Fenn.* **53**, 165 (1964). For a complete review of physiological abnormalities associated with blindness, see F. Hollwich, *The Influence of Ocular Light Perception on Metabolism in Man and in Animal* (Springer-Verlag, New York, 1979), pp. 17–87.
27. F. Hollwich, in (*26*), pp. 75–77; C. A. Elden, *Nippon Funin Gakkai Zasshi* **16**, 48 (1971).
28. D. N. Orth and D. P. Island [*J. Clin. Endocrinol. Metab.* **29**, 479 (1969)] reported that the 24-hour rhythm of cortisol secretion in humans can be entrained by the light-dark cycle. F. Hollwich and B. Dieckhues [*Klin. Monatsbl. Augenheilkd.* **15**, 11 (1968)] reported that short-term exposure to light suppresses the peripheral eosinophil count. This effect might be the result of a hypothalamic-pituitary-adrenal response to stress (*26*, pp. 48–54 and 78–88). Stress does not seem to affect melatonin secretion [(*10*); G. M. Vaughan, S. D. McDonald, R. M. Jordan, J. P. Allen, G. L. Bohmfalk, M. Abou-Samra, J. L. Story, *J. Clin. Endocrinol. Metab.* **47**, 220 (1978)]. Furthermore, the effect, if any, of stress would be an increase in melatonin concentrations [A. G. Parfitt and D. C. Klein, *Endocrinology* **99**, 840 (1976)].
29. R. Y. Moore, in *Endocrine Rhythms*, D. T. Krieger, Ed. (Raven, New York, 1979), p. 63. An area in the human brain which is anatomically homologous to the SCN has been described [R. Lydic, W. C. Schoene, C. A. Czeisler, M. C. Moore-Ede, *Sleep*, in press; R. Y. Moore, personal communication].
30. K. E. Klein and H.-M. Wegmann, in *Chronobiology*, L. E. Scheving, F. Halberg, J. E. Pauly, Eds. (Igako Shoin, Tokyo, 1974), p. 564.
31. We thank J. O'Steen, M. Webster, C. Craig, C. Crawford, and D. McKenzie.
* Correspondence should be addressed to A.J.L.

12 August 1980

Glucose Suppresses Basal Firing and Haloperidol-Induced Increases in the Firing Rate of Central Dopaminergic Neurons

Abstract. *In the rat, doses of glucose sufficient to raise glucose concentrations in the blood to levels equivalent to those produced by a meal or stress suppress the firing of dopamine-containing neurons located within the substantia nigra. Glucose also prevents or reverses the increase in discharge rates of dopaminergic cells normally elicited by the antipsychotic agent haloperidol.*

Central dopamine-mediated systems play an important role in maintaining motivated feeding behaviors especially in response to abrupt decreases in glucose use (*1*). We now report that glucose administration suppresses the firing of central dopaminergic neurons within the zona compacta of the substantia nigra (SNC). These findings are perhaps related to the broad influence of these neurons on motor, sensory, and cognitive functions (*2*).

Male albino Sprague-Dawley rats (175 to 350 g, Zivic-Miller) were housed two per cage and maintained on an alternating 12-hour light-dark cycle with free access to food and water. Animals were anesthetized with chloral hydrate (400 mg per kilogram of body weight) and mounted in a stereotaxic apparatus. A recording micropipette filled with 2*M* NaCl saturated with Fast Green dye (in vitro impedance, 2 to 10 megohms) was lowered into the region of the SNC [anterior, 1300 to 2400 μm; lateral, 1300 to 2400 μm (*3*)], and single unit activity was recorded (*4*). Dopaminergic neurons were located on the basis of previously described electrophysiological criteria (*5*). Briefly, these neurons have spontaneous firing rates of 1 to 9 Hz, often display a train of action potentials or "bursts" upon discharge, have biphasic waveforms (positive or negative) with amplitudes of 0.4 to 1.5 mV, and durations as long as 4 msec. All control cells (dopaminergic neurons tested with hypertonic saline, L-glucose, or D-fructose) also met the pharmacological criteria for mesencephalic dopaminergic cells (*5*). That is, their firing rates were slowed by the administration of a dopamine agonist (amphetamine) and increased by a dopa-

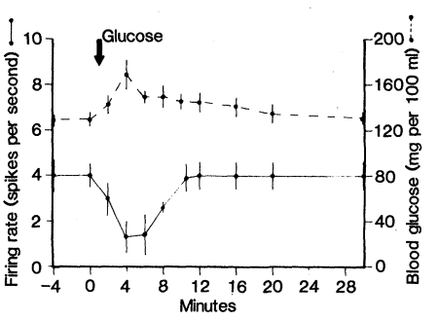

Fig. 1. Changes in the spontaneous activity of dopamine-containing neurons located within the SNC (mean ± standard error, $N = 6$) and blood glucose ($N = 8$) after the administration of D-glucose (15 mg/kg, intravenous).

0036-8075/80/1212-1269$00.50/0

mine antagonist (haloperidol). In all cases only one cell was sampled per animal. At the end of each recording session, the site of the micropipette was marked by passing a 40-μA cathodal current for 10 minutes. The animals were then perfused and their brains removed for histological verification of the electrode placement.

Glucose or equiosmolar volumes of saline were administered through femoral vein catheters. Intravenous glucose (250 mg/kg) inhibited the activity of all dopaminergic neurons sampled (N = 12). The onset of this decrease in activity began approximately 1 to 3 minutes after glucose administration; cell discharge ceased completely 3 to 7 minutes after injection. The individual action potentials of these neurons changed just before the inhibition of activity. That is, the waveforms became slightly irregular while displaying an increase in duration and a decrease in amplitude. Inhibition of spontaneous activity and similar waveform alterations were also seen after subcutaneous glucose administration (250 mg/kg, N = 6). With both intravenous and subcutaneous injections, the neuronal activity was completely inhibited for at least 30 minutes, after which the recording sessions were terminated.

A lower dose of glucose (15 mg/kg, intravenous, N = 6) also inhibited the activity of dopaminergic neurons. The spontaneous activity of three of these cells was totally inhibited, and that of the other three reduced by 60 to 85 percent (Fig. 1). We also examined the effects of this dose of glucose on the blood glucose concentrations of animals anesthetized with chloral hydrate (N = 8). Blood was collected 4 minutes before glucose administration and 2, 4, 6, 8, 10, 12, 16, 20, and 30 minutes thereafter (*6*). Blood glucose concentrations were maximally elevated (by approximately 30 percent) at 4 minutes and quickly returned to pre-injection levels (Fig. 1). The inhibition of dopaminergic neural activity lasted for 4 to 10 minutes, which corresponds to the period of elevated blood glucose. The activity of additional dopaminergic neurons was not inhibited by the intravenous administration of either an equiosmolar solution of saline (N = 4) or the nonmetabolizable L-isomer of glucose (150 mg/kg, intravenous, N = 5). Furthermore, fructose (15 mg/kg, intravenous, N = 6; 150 mg/kg, intravenous, N = 3), a sugar not readily used by the brain in vivo (*7*), did not alter dopaminergic neuronal discharge. All of these control cells met the previously described pharmacological criteria for dopaminergic neurons. They were inhibited by the administration of amphetamine (1.0 to 2.0 mg/kg. intravenous) and subsequently increased their activity in response to haloperidol (0.1 to 0.3 mg/kg, intravenous).

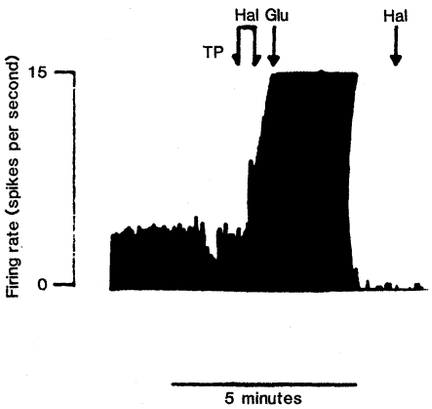

Fig. 2. Cumulative frequency histogram of a single dopaminergic neuron illustrating the increase in firing rate produced by haloperidol (*Hal*; 0.2 mg/kg) and the suppression of cell activity 2.5 minutes after D-glucose administration (*Glu*; 250 mg/kg). A second haloperidol injection (0.2 mg/kg) during this period of glucose-induced suppression was unable to reverse this effect. Each vertical pen deflection equals a 5-second average of neural activity. Arrows indicate the intravenous administration of pharmacological agents. This neuron was also responsive to sensory stimuli-mild tail pressure (*TP*) (*4*).

We then asked if glucose inhibited dopaminergic cell discharge by directly or indirectly stimulating the release of dopamine, since such stimulation suppresses impulse flow in dopaminergic neurons (*8*). We thus examined the effects of glucose in rats administered the dopamine antagonist haloperidol (*9*). In agreement with previous findings (*5*), haloperidol (0.1 to 0.5 mg/kg, intravenous, N = 10) considerably increased dopaminergic cell activity (pharmacologically confirming their dopaminergic nature). The subsequent administration of glucose (250 mg/kg, intravenous) again totally inhibited the discharge rates of all dopaminergic neurons sampled (Fig. 2). Furthermore, this inhibition could not be reversed by the additional administration of haloperidol (0.2 to 0.5 mg/kg, intravenous). Therefore, it seems unlikely that glucose blocks dopaminergic neuronal discharge by stimulating dopamine receptors. All dopaminergic neurons reported above were histologically located within the SNC.

In the course of these investigations, recordings were also made from nondopaminergic neurons located in the zona reticulata of the substantia nigra (N = 11). None of these cells changed their firing rates after glucose was administered (250 mg/kg, intravenous). Neurons sampled in the red nucleus were also unresponsive to glucose treatment (N = 4). The spontaneous activity of lateral hypothalamic neurons is also suppressed by glucose (*10*). It may be of note that mesencephalic dopaminergic neurons project through this region (*2*).

The effects of glucose administration on dopaminergic activity appear attributable to glucose, rather than some artifact of the injection procedure. Thus, the osmolarity of the glucose solutions injected was not a significant factor, since neither equiosmolar saline nor L-glucose inhibited dopaminergic cell activity (*11*). The delay in the cessation of dopaminergic activity for at least 3 minutes after intravenous injection also indicates that the effects are a result of some metabolic action of glucose. In addition, the changes in the waveform accompanying the reduction of activity suggests a local action at the level of the dopaminergic neurons.

The findings that fructose did not change the discharge rates of dopaminergic cells provides some insights into the mechanisms by which glucose may affect dopaminergic activity. Fructose and glucose can be used as fuels by most peripheral tissues, but fructose is not readily used by the brain in vivo (*7*). Therefore, receptors sensitive to changes in peripheral energy metabolism are probably not involved in changing dopaminergic firing. Insulin, however, may play some role in mediating the effects of glucose on dopaminergic activity. Fructose is much less effective than glucose in promoting insulin release (*12*). Consequently, glucose-induced increases in insulin secretion may be ultimately responsible for the changes in dopaminergic transmission. For example, insulin might alter dopaminergic transmission by directly affecting cerebral metabolism by stimulating cerebral insulin receptors (*13*). Likewise, glucose or insulin may alter the metabolism of other central neurotransmitter systems, which in turn may modulate central dopaminergic activity (for example, γ-aminobutyric acid, glycine, serotonin) (*14*). It is also possible that glucose may directly alter the metabolism of central dopamine-containing neurons. Thus, we have found that the waveform of the action potential of dopaminergic neurons is altered after glucose administration; glucose has been reported to increase synaptosomal dopamine uptake and tyrosine hydroxylase activity (the rate-limiting enzyme in dopamine synthesis) (*15*).

It seems likely that the effects of glu-

cose on central dopaminergic transmission are physiologically relevant. The lower dose of glucose (15 mg/kg, intravenous) elevated blood glucose concentrations by only 30 to 40 mg per 100 ml of blood. Food consumption or the mobilization of liver glycogen during stress can produce similar elevations (*16*). Moreover, the length of time dopaminergic activity is suppressed after a 15-mg/kg dose of glucose appears to coincide with the period of elevated blood glucose concentrations. Thus, daily physiological fluctuations in glucose availability may significantly influence dopamine-mediated activity in the brain.

CHARLES F. SALLER
Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland 20205
LOUIS A. CHIODO
Psychobiology Program, Department of Psychology, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

References and Notes

1. M. J. Zigmond and E. M. Stricker, *Science* **177**, 1211 (1972); T. G. Hefner, M. J. Zigmond, E. M. Stricker, *J. Pharmacol. Exp. Ther.* **201**, 386 (1977).
2. R. Y. Moore and F. E. Bloom, *Annu. Rev. Neurosci.* **1**, 129 (1978); A. Dray, *Neuroscience* **4**, 1407 (1979); S. Matthysse, in *The Neurosciences: Third Study Program*, F. O. Schmitt and F. G. Worden, Eds. (MIT Press, Cambridge, Mass., 1974), p. 733.
3. J. F. R. Konig and R. A. Klippel, *The Rat Brain: A Stereotaxic Atlas* (Williams & Wilkins, Baltimore, 1974).
4. L. A. Chiodo, A. R. Caggiula, S. M. Antelman, C. G. Lineberry, *Brain Res.* **176**, 385 (1979); L. A. Chiodo, S. M. Antelman, A. R. Caggiula, C. G. Lineberry, *ibid.* **189**, 544 (1980).
5. B. S. Bunney and G. K. Aghajanian, in *Antipsychotic Drugs: Pharmacodynamics and Pharmacokinetics*, G. Sedvall, B. Urnas, Y. Zotterman, Eds. (Pergamon, New York, 1976), pp. 305-318.
6. Blood (50 to 100 μl) was collected into heparinized tubes from cannulas inserted into the tail artery. Duplicate 10-μl portions of blood were immediately deproteinized with barium hydroxide and zinc sulfate and assayed for glucose content [M. E. Wahko and E. W. Rice, *Clin. Chem. (Winston-Salem, N.C.)* 7, 542 (1961)].
7. R. J. Klein, R. Hurwitz, N. S. Olsen, *J. Biol. Chem.* **164**, 509 (1946); C. R. Park, L. H. Johnson, J. H. Wright, Jr., H. Bastel, *Am. J. Physiol.* **191**, 13 (1957); W. H. Oldendorf, *ibid.* **221**, 1629 (1971); G. Hetenyi, Jr., *Diabetes* **21**, 797 (1972). Manose (25 mg/kg, intravenous, $N = 3$), which can be utilized by the brain, also inhibited dopamine-mediated neuronal activity.
8. L. I. Iversen, M. A. Rogawski, R. J. Miller, *Mol. Pharmacol.* **12**, 251 (1976); G. K. Aghajanian and B. S. Bunney, *Naunyn-Schmiedebergs Arch. Pharmakol.* **304**, 255 (1978); P. M. Groves, C. J. Wilson, S. J. Young, G. V. Rebec, *Science* **190**, 522 (1975).
9. Biochemical evidence indicates that even the lowest dose of haloperidol used should have almost totally blocked dopaminergic receptors [A. Carlsson, *Biol. Psychiatry* **13**, 3 (1978)].
10. B. K. Anand, G. S. K. N. Chhina, S. Dua, B. Singh, *Am. J. Physiol.* **207**, 1146 (1964).
11. A brief increase in neuronal discharge was observed in a subgroup of dopaminergic cells immediately after the subcutaneous administration of glucose or saline. These cells were type A neurons (*4*), which increase their firing in response to activating sensory stimuli. This effect lasted for 30 to 60 seconds and was presumably due to local irritation at the site of injection.
12. J. M. Atken and M. G. Dunnigan, *Br. Med. J.* **3**, 276 (1969).
13. J. Haurankova, J. Roth, M. Brownstein, *Nature (London)* **272**, 827 (1978); J. Haurankova, D. Schmechel, J. Roth, M. Brownstein. *Proc. Natl. Acad. Sci. U.S.A.* **75**, 5737 (1978).
14. M. K. Gaitonde, D. R. Dahl, K. A. C. Elliott, *Biochem. J.* **94**, 345 (1965); L. D. Lewis, B. Ljunggren, K. Norberg, B. K. Siesjo, *J. Neurochem.* **23**, 659 (1974); V. Leviel, A. Chermay, A. Nieoullon, J. Glowinski. *Brain Res.* **175**, 259 (1979); A. Dray, J. Davies, N. R. Oakley, P. Tongrach, S. Vellucci. *ibid.* **151**, 431 (1978); J. D. Fernstrom and R. J. Wurtman, *Science* **174**, 1023 (1971).
15. R. L. Dorris, *Neuropharmacology* **17**, 157 (1978); S. Psychonyos, B. R. Stanton, C. D. Atkins, *Life Sci.* **25**, 1119 (1979).
16. The consumption of a meal by a normally feeding rat raises blood glucose concentrations by 20 to 30 mg per 100 ml [A. B. Steffens, *Physiol. Behav.* **4**, 823 (1969); J. H. Strubbe, A. B. Steffens, L. DeRuiter, *ibid.* **18**, 81 (1977)]. We have found that blood glucose levels are also elevated by 20 to 40 mg per 100 ml during restraint or after a meal in rats deprived of food overnight.
17. We thank I. J. Kopin, E. M. Stricker, A. R. Caggiula for their comments on the manuscript and D. Shirk for manuscript preparation. Supported by The National Institute of General Medical Sciences Pharmacology Research Associate Program (C.F.S.), and National Institute of Mental Health grants 5T 32-MH14634 and MH 16581 (L.A.C.).

1 February 1980; revised 17 June 1980

Fasting Associated with Decrease in Hypothalamic β-Endorphin

Abstract. *In rats that were fasted for 2 to 3 days there was a decline in hypothalamic, but not pituitary, β-endorphin. There was no change in pituitary or hypothalamic adrenocorticotropin content as a result of fasting. Endogenous opiates may be involved in physiological adaptation to fasting.*

Organisms conserve energy during fasting in part by lowering the serum concentration of 3,5,3′-triiodothyronine (T_3) and concomitantly increasing the concentration of 3,3′,5′-triiodothyronine (reverse T_3) (*1*, *2*), the latter having little or no calorigenic activity. In anticipation of famine, hibernating animals accumulate extra calories either by increasing food intake and thus adipose tissue stores or by hoarding food in their nest (*3*). Hibernation and fasting both result in a state of anorexia (*3*), which may be an adaptation to prevent food-seeking energy expenditure until a time when food is plentiful.

β-Endorphin, an endogenous opiate found primarily in the central nervous system and anterior pituitary (*4*), stimulates food intake when administered intraventricularly (*5*). Concentrations of β-endorphin are increased in pituitaries from genetically obese mice and rats (*6*, *7*). Naloxone, an opiate antagonist, suppresses spontaneous food intake and weight gain when administered subcutaneously to normal rats (*8*), normalizes food intake in genetically obese rodents (*9*), and awakens hibernating animals (*10*). In the present study our purpose was to determine whether fasting affects the concentration of β-endorphin in the anterior pituitary or hypothalamus, areas that are rich in this opiate and that have been linked with the regulation of feeding behavior.

Male Sprague-Dawley rats (225 to 250 g) were housed at 22°C with a 12-hour dark-light cycle in individual cages for 1 week, during which time they received daily handling and free access to food and water. They were then divided into four groups, and food was withheld from three of the four groups for 1, 2, or 3 days.

On the morning of study, the animals were decapitated, and the hypothalamus and pituitary were rapidly removed. The posterior pituitary was gently removed from the remaining pituitary with an ophthalmic forceps and discarded. The tissues were then homogenized in buffer (0.05*M* PO_4, 0.15*M* NaCl, *p*H 7.4, with 1 m*M* *N*-ethylmaleimide, a potent peptidase inhibitor) at 4°C (*4*, *5*, *11*) with a Brinkmann polytron at setting 6 for 10 seconds. β-Endorphin was measured by radioimmunoassay based on the method of Guillemin *et al.* (*12*) with an antibody that has an approximate 10 percent cross-reactivity with human β-lipoprotein but no cross-reactivity with adreno-

Table 1. Effect of fasting on central nervous system β-endorphin. Values represent means ± standard deviation. Nonsignificant = $P > .05$; P values represent comparisons of fasted animals to nonfasted controls (unpaired t-test). N.S., not significant.

Animal	N	β-Endorphin (nanograms per milligram of protein)			
		Hypothalamic		Pituitary	
		Concentration	P	Concentration	P
Control	20	3.45 ± 1.7		1,510 ± 998	
Fasted 1 day	12	3.40 ± 0.4	N.S.	1,151 ± 518	N.S.
Fasted 2 days	7	1.69 ± 0.8	< .02	1,231 ± 592	N.S.
Fasted 3 days	12	1.22 ± 0.3	< .01	1,171 ± 542	N.S.

0036-8075/80/1212-1271$00.50/0