Thus, our results support some of the criticisms of the surveillance theory (*18*). On the other hand, according to the recently proposed "immune stimulation" theory (*19*), the *nu/nu* mice may have fewer tumors than their normal counterparts. This was not the case for the fibrosarcomas, although a slight decrease in the incidence of lung adenomas was observed in the *nu/nu* mice (see Table 2).

The relatively high incidence of lymphomas as well as epithelial solid tumors in humans with primary immune deficiencies (*20*) or in patients undergoing prolonged immunodepression for transplantation (*21*) suggests that an intact immune system may play an active role controlling malignant development (*4*). On the other hand, such association has not been observed in other immune deficiencies such as leprosy or some autoimmune disorders (*22*), while others contend that the high incidence of lymphomas in those patients may be a result of either the primary disease or the administered drugs (*18*).

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Piperidine Increase in the Brain of Dormant Mice

Abstract. *During a 2-hour period of dormancy (sleep), piperidine is accumulated in the mouse brain.*

Piperidine has been shown to have transmitter-like pharmacological properties in the molluscan central nervous system (*1*); it is physiologically present in the brains of many species including man (*2*). Some tissues of the mammalian brain were also reported to contain relatively greater quantities of piperidine than other tissue (*3*). The piperidine concentration in the brain of snails during experimentally induced hibernation increases severalfold (*4*), and piperidine might be involved in the process of hibernation in snails (*1*, *4*). We now report on piperidine measurements in the mouse brain, which were performed to determine whether any appreciable change in its concentration in mammalian brain can be detected during diurnal variations of behavioral activity.

Forty inbred female mice (3 months old) strain C57B1/6, were caged for 1 week, under constant illumination, before the experiment. Ten animals were randomly selected as "active" at a time when all animals were active; of the remaining mice, ten were randomly chosen as "dormant" at a time when all mice had been dormant for at least 2 hours. Since there is no absolute behavioral criterion of sleep (*5*), we refer here to a dormant mouse as

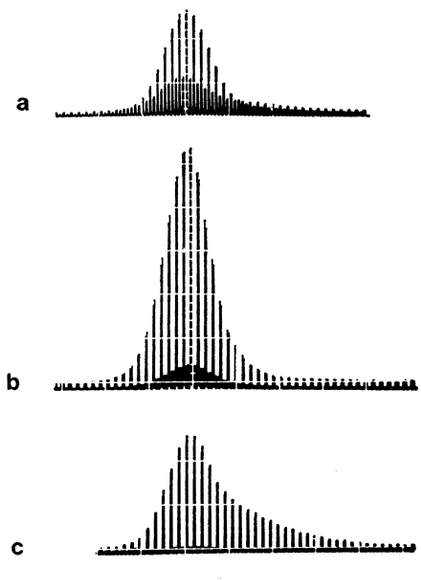

Fig. 1. Quantitative mass spectrometric measurement of piperidine. Evaporation profiles of dansylated pyrrolidine as an internal standard (1.65×10^{-10} mole in each sample), and dansylated piperidine from the mouse brain. The ion currents for *m/e* 304 and 318 were consecutively displayed on an oscilloscope (the two envelope curves in each record). In records (a) and (c) the pyrrolidine curves are higher than those of piperidine; in record (b) the piperidine curve is higher than the pyrrolidine standard. The records are from (a) brain of an active mouse, (b) brain of a dormant mouse, and (c) piperidine blank sample without tissue (the piperidine curve reaches only slightly above the lowest white line of the graticule). Relative amplifications are: (a) 4×; (b) 1×; and (c) 5×; time base, 15 seconds per division.

one having a posture characteristic of sleep, with its eyes closed, crouching or lying with the other dormant mice. In contrast to our report on hibernating mollusks (*4*), the term "dormant" does not imply any hibernating mechanism, and the term "active" is used here to describe an animal that is moving in the cage, eating, and drinking.

Within 5 seconds after being removed from the cage, the animals were killed by cervical dislocation and decapitated. The whole brain was removed, blotted, weighed, and homogenized in ice-cold 0.2*M* perchloric acid. The steps from decapitation through homogenization were performed in about 1 minute for each brain. The determination of piperidine has been described (*4*). The whole homogenate was submitted to dansylation (dimethylaminonaphthalenesulfonyl chloride) (*6*). The dansyl derivatives were extracted into an organic solvent and separated by one-dimensional chromatography on silica gel with the solvent system cyclohexane–butyl acetate (2 : 1). The fraction which cochromatographed with standards of dansylated piperidine was scraped off and its piperidine content was measured by the mass spectrometry (*7*). A known quantity of dansylated pyrrolidine was added as an internal standard to the sample, and the mixture was introduced into the mass spectrometer (AEI model MS-902) and "flash" evaporated. The ion currents corresponding to dansylated pyrrolidine (*m/e* 304) and dansylated piperidine (*m/e* 318) were recorded with the use of the peak matching circuit of the spectrometer at a resolving power of about 2000 (Fig. 1). The actual quantity of piperidine in each sample was calculated from the area ratio of recorded currents between the known quantity of pyrrolidine and the unknown quantity of piperidine.

The piperidine concentration in the brain rose during dormancy to 36.6 ± 6.35 pmole/mg ($N = 10$), compared to 2.00 ± 0.55 pmole/mg ($N = 10$) found in active animals ($P < .001$). The weight of the brain was unchanged during the same interval (dormant: 405 ± 11 mg; active: 395 ± 8.3 mg). This unexpected increase in apparent piperidine concentration in the dormant mouse brain exceeded by several times any previously reported concentration of piperidine in the brain, or in any of its assayed components (*2–4*). The piperidine content found in the brain of active mice, however, concurs well with the measurements of others. It should be noted that our values have not been corrected for losses during extraction and thin-layer chromatography.

It is premature to discuss this finding in view of the scarcity of data on the direct effect of piperidine on mammalian nerve cells (*8*). The known pharmacological effects are mostly only peripheral or peripherally induced (*9*), and there is no reliable information as to the passage of administered piperidine either from the blood or from the cerebrospinal fluid into the brain tissue (*10*). However, in view of the similarity between piperidine action (*1*), its accumulation in dormant mollusks (*4*), and our data, one might expect that piperidine will be somehow connected with the sleep-wakefulness mechanisms in the mouse.

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Serotonin Storage in Platelets: Estimation of Storage-Packet Size

Abstract. *Storage-body diameter and volume, and the number of molecules of serotonin contained in a storage body, were estimated for blood platelets. In the human, 5.23 × 10^5 molecules of serotonin are contained in a storage body 198 nanometers in diameter, while in the cat, 31.2 × 10^5 molecules of this amine are contained in a storage body 298 nanometers in diameter.*

In platelets, serotonin is believed to be stored in discrete, membrane-bound organelles ("dense bodies"), probably complexed with adenosine triphosphate (ATP), divalent ions, and possibly a small amount of protein (*1*). Platelet serotonin, ATP, and divalent ions are released by thrombin in what appears to be an all-or-none process with a rapid time course (*2*). This release process may occur by exocytosis of the contents of individual storage bodies, in a fashion analogous to amine release from vesicles in the adrenal medulla and noradrenergic nerves (*3*).

Table 1. Serotonin storage in human and cat platelets (mean ± standard error of the mean).

Item	Human	Cat
Platelet		
Serotonin (10^6 molecules)	3.65 ± 0.28	35.4 ± 4.1
Storage bodies (No.)	6.4 ± 0.3	12.1 ± 0.6
Storage body		
Serotonin (10^5 molecules)	5.23 ± 0.69	31.2 ± 6.4
Diameter (nm)	198 ± 6	298 ± 7
Volume (10^6 nm^3)	6.69 ± 0.77	16.3 ± 1.1

In chemically transmitting nerve endings, it has proved useful to define a "storage packet" as the amount of transmitter released from a single membrane-limited vesicle. Adopting this terminology, we sought to estimate storage-packet size in serotonin-containing storage bodies from isolated platelets, in order to assist in the pharmacological and physiological evaluation of platelet function. In view of the many similarities between platelets and other amine-storing systems (*4*), the results may contribute to our understanding of secretory processes in general.

Platelet-rich plasma (PRP) and platelet pellets were prepared from human and cat blood (*5*). Portions of each sample were taken for platelet counts (*6*) and serotonin assay (*7*). In order to