Thus it is the *corrected* value of T, T_{corr}, as given by Eq. 3, that is linear in $(a + b)/a \propto x$ (note that a remains fixed as water is added, and $a + b$ is the total weight of the water).

To test this, values of T_{obs} were taken from figure 2B of (*1*); the corresponding corrected values were then calculated from Eq. 3 with $T_b = 2500$ msec. In Fig. 1 we plot T_{corr} versus x; also shown are the original data. It is our contention that the corrected graph supports the linear theory.

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In our report (*1*), we did not consider it necessary to present a detailed analysis of T_1 as a function of cellular hydration as suggested by Brownstein and Tarr for three reasons. First, a plot of $1/t_{1(obs)}$ versus $1/x$ (where x is grams of H_2O per gram of dry solids) did not prove to be linear over the entire range of hydration. Second, Raaphorst *et al.* have shown that, as the concentration of water in CHO cells is decreased, the T_1 values for the water protons first decrease and then increase [see figure 3 of (*2*)]. Third, the relaxation times of water protons were shown to change independently of cellular hydration during the HeLa cell cycle [see figure 2A of (*1*)].

The analysis of Brownstein and Tarr demonstrates a linear relationship between their T_{corr} and hydration over the range of 4 to 8 g of H_2O per gram of dry solids. Above 8 g of H_2O per gram of dry solids, there is a change in slope (see their figure). This is the exact observation we made. Therefore, their comment does not add anything new.

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23 August 1976

Serotonin Depression

Åsberg *et al.* (*1*) have observed that the distribution of spinal fluid 5-hydroxyindoleacetic acid (5-HIAA) in some depressed patients was bimodal and inferred that there may be a subgroup of patients with "serotonin depression." There are alternative explanations for this result.

Brain serotinin is known to have a very large 24-hour rhythm (*2*), comparable to the range of variation noted by Åsberg *et al.* Furthermore, there has been speculation that the phase of 24-hour rhythms may be altered in depressed patients. The bimodal distribution reported by the authors could thus be caused by a bimodal distribution in the phases of 24-hour serotonin rhythms without any alteration in total 24-hour serotonin turnover. Furthermore, since one obtains a bimodal distribution by sampling any sinusoidal or square-wave rhythmic function at random phases, a similar result might be obtained if the phases of 24-hour serotonin rhythms were random in depressed patients and uncoupled from social synchronizers.

There is evidence that serotonergic neurons mediate the appearance of slow-wave sleep (*3*). Many depressed patients may sleep poorly at night, but some also nap during the day. Therefore, if a rhythm disturbance is critical, one might expect 5-HIAA levels to correlate better with measures of sleep than with the overall depression ratings, especially correlating cerebrospinal fluid (CSF) 5-HIAA with the amount of sleep in the hours immediately before the CSF sample is obtained. While it would be most interesting to quantify slow-wave sleep electroencephalographically, it might be sufficient to estimate the patients' sleep subjectively to test whether sleep timing accounts for the heterogeneity of CSF 5-HIAA in depressed subjects.

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12 March 1976; revised 21 July 1976