ficient to produce the phenomenon. Indeed, only when both NE and DA were depleted in the striatum and cortex did the excessive abnormal walking appear in response to blockade of acetylcholine.

Neither an acetylcholine-DA interaction nor an acetylcholine-NE interaction alone can account for all the complexities of the phenomenon we have reported. For instance, an additional group (see NE < DA in Tables 1 and 2), though not akinetic (their locomotion seemed relatively normal when no drug was administered), walked excessively in response to atropine, using normal-sized steps and even running in the activity wheel (*7*). Only when striatal dopamine was also severely depleted (NE-DA) did the short-step aspect of the excessive walking appear (*8*). Atropine seems to interact with both NE and DA in ways and at sites that remain to be more fully understood (*9*). Such understanding will proceed only if brain neurochemistry is done hand in hand with adequate behavioral analysis.

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References and Notes

1. T. Schallert, I. Q. Whishaw, V. D. Ramirez, P. Teitelbaum, *Science* **199**, 1461 (1978).
2. We did not "claim . . . evidence for an interaction solely with dopamine."
3. D. R. Levitt and P. Teitelbaum, *Proc. Natl. Acad. Sci. U.S.A.* **72**, 2819 (1975); I. Golani, D. L. Wolgin, P. Teitelbaum, *Brain Res.*, in press; P. Teitelbaum, T. Schallert, M. De Ryck, I. Q. Whishaw, I. Golani, in *U.S.A.-U.S.S.R. Symposium on Neurophysiological Mechanisms of Goal-Directed Behavior and Learning*, R. F. Thompson, Ed., in press; T. Schallert, M. De Ryck, I. Q. Whishaw, V. D. Ramirez, P. Teitelbaum, *Exp. Neurol.*, in press.
4. Note that the cortical NE values for the two techniques were comparable (Table 1). For the DB group, we injected 4 μg of 6-OHDA locally into the dorsal noradrenergic bundle in four rats and 8 μg in four additional rats (the data for the two doses were pooled because the results were similar). For group NE-DA, seven rats were treated with large doses of 6-OHDA intraventricularly (200 μg into each lateral ventricle and 100 μg into the third ventricle). Treatment with pargyline (50 mg/kg) preceded the 6-OHDA treatment in two of these rats.
5. By a step, we mean the average distance between two successive footprints made by the same hindleg on one side of the body.
6. In the DMI group, three rats received intraperitoneal injections of DMI (25 mg/kg) and pargyline (50 mg/kg) 30 minutes prior to receiving intraventricular injections of 6-OHDA (the same dose as group NE-DA).
7. In the NE < DA group, four rats were treated intraventricularly with smaller doses of 6-OHDA (100 μg into both lateral ventricles) with no special prior treatment.
8. Median step sizes were: control, 14.4 cm; DB, 14.6 cm; NE-DA, 9.0 cm; DMI, 5.0 cm; and NE < DA, 14.6 cm.
9. For example, brainstem or spinal mechanisms may also be involved. In our study, the two groups that were the most active after atropine treatment (group NE-DA and group NE < DA) showed little or no convulsive kicking behavior when they were decapitated. All rats in groups DMI and DB, which did not show hyperactivity to atropine, showed the prolonged rapid and powerful decapitation-released kicking behavior that occurs in control animals. Thus, the lack of kicking was not correlated with degree of akinesia (which presumably is a striatum-related effect) but seemed to be correlated with the propensity to show atropine-induced hyperactivity in the wheel. Although the hyperkinesia induced by atropine in group NE < DA was blocked by haloperidol (2 mg/kg, a dopamine receptor blocking agent), it was not blocked by haloperidol in group NE-DA, in which striatal dopamine was even more severely depleted. The role of other transmitters should be explored.
10. I. Q. Whishaw, T. E. Robinson, T. Schallert, M. De Ryck, V. D. Ramirez, *Exp. Neurol.*, in press.
11. This study was supported by National Research Council of Canada grant A8273 to I.Q.W., NIH grant R01 NS 11671 and University of Illinois biomedical research grant to P. T., and University of Illinois biomedical research grant to V.D.R. We thank R. Dodic and N. Peshkin for help with animal care and D. Kassner-Whelchel for typing the manuscript.

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Age Affect and Replicative Life-Span of Fibroblasts of Diabetic, Prediabetic, and Normal Donors: Another Look at the Data

The purpose of this technical comment is twofold. The first is to correct some numerical and biostatistical errors in our recent report (*1*). The second is to describe the results of further analysis of the data.

The statistical methods used were not described in (*1*) and are outlined here for clarification. Pearson's correlation was used to calculate the relation between age of donor (x) and total mean population doublings (y). Linear regression was used to fit a least-squares line to the data. Comparisons among the mean replicative life-spans were made by one-way analysis of variance followed by unpaired t-tests between all pairs of means corrected for degrees of freedom. A test for linear trend among group means was also performed. We performed the analyses on an IBM 370/168 computer using the Data-Text program package (*2*).

Tables 1 and 2 summarize the previously reported data with corrections as indicated. With reference to the text of the previous report, two corrections should be noted. In the first paragraph of the first column of page 782 (*1*) the linear trend was not significant ($P = .215$) as indicated, and therefore does not support the hypothesis of progressive decrease in replicative capacity with increasing predisposition to diabetes. Then in the middle of the second column on the same page, the statement should have indicated the lack of a *significant negative* correlation between age and total mean population doublings in the normal group rather than implying lack of a negative value when it was indeed present, but not statistically significant.

The presence of these errors was unfortunate; we thank Senner (*3*) for causing us to review the data analyses again. Other problems were noted as indicated in Tables 1 and 2 and have now been corrected.

Although the mean ages did not differ significantly among the three study groups, the age ranges and age distribu-

Table 1. Summary of previously reported data (*1*).

Study group	N	r	Regression line (x = age, y = total mean population doublings)	P
Normals	25	−.279*	$y = 59.47^* - .17x^*$	.177
Prediabetics	21	−.579*	$y = 66.57 - .46x$	.006*
Diabetics	26	−.431*	$y = 59.31^* - .29x^*$	.020*
Combined	72	−.392*	$y = 60.47^* - .27x^*$	.001

*Values that were in error in (*1*).

Table 2. Summary of previously reported data (*1*) (means ± standard deviation).

Study group	Age (years)	Age range (years)	Total mean population doublings	Total mean population doublings adjusted for age
Normals	44.3 ± 17.5	15 to 76	51.76 ± 10.92	52.54 ± 11.05
Prediabetics	40.0 ± 15.0	19* to 62	48.29* ± 11.88	47.84 ± 10.88
Diabetics	40.2 ± 19.2	14 to 76	47.54 ± 13.10	47.14 ± 11.02

*Values that were in error in (*1*).

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tions were not identical. Therefore, the correct way to examine the data is to compare the mean replicative life-spans after adjusting for age. This was accomplished by analysis of covariance (*4*).

The first step was to determine if the relation between age and mean total population doublings differed among the three populations. In other words, were the slopes of the linear regression lines significantly different. The results indicated that they were not ($P = .4$), thus making it possible to combine the three groups and to calculate a common regression line which had a slope significantly different from zero ($P = .0003$).

After noting the significant decline in mean total population doublings with age, we tested to see if, as the predisposition to diabetes mellitus increased, the age-adjusted mean total population doublings decreased. This was accomplished by testing for the statistical significance of the linear contrast among the adjusted means. Since we are testing the hypothesis that the fibroblast life-spans for diabetics < prediabetics < normals, a single-tailed *t*-test was used. The results indicated that the fibroblast replicative life-span did decline with increasing predisposition to diabetes ($P = .04$). Although these studies need corroboration by other investigators using larger sample sizes, they do provide sufficient evidence to indicate that this phenomenon warrants further consideration.

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Carnivoran Jaw Shape

In a discussion of the evolution of New World dogs, Olsen and Olsen (*1*), note that the "turned-back" apex of the mandibular coronoid process, which results in an "overhang" of bone along the caudal or back edge of the coronoid process, is a diagnostic feature of domesticated dogs (*Canis familiaris*). They state that dogs have this feature, whereas other canids generally do not. They also state that the turned-back coronoid process of domestic dogs and the Chinese wolf (*Canis lupus chanco*) may indicate that these forms were "omnivorous" carnivorans, rather than strict meat eaters. Their notion that the shape of the carnivoran coronoid process is an indicator of diet is based on the following observation: "In the true 'meat eating' carnivores, such as cats (*Felidae*), there was no overhang in this area. The apex [referring to the coronoid process] was terminated in a symmetrically rounded crest. The same was true of the badgers and otters (*Taxidea* and *Lutra*, respectively). However, there was a noticeable overhang, similar to that in dogs, in carnivores with an omnivorous diet, as in bears (*Ursidae*)" (*1*, p. 535).

The notion that the turned-back coronoid process of carnivorans is a reliable indicator of an omnivorous diet is incorrect. Although ursids may have a turned-back coronoid process, not all ursids are omnivorous. The giant panda (*Ailuropoda melanoleuca*), thought by many to be an ursid (*2, 3*), has a diet that consists primarily of bamboo shoots (*4*), whereas the polar bear (*Thalarctos maritimus*) has a diet that consists almost entirely of fish and seals (*5*); yet both have turned-back coronoid processes (*2*) (Fig. 1). Moreover, other highly carnivorous carnivorans have turned-back coronoid processes. For example, jaguars (*Felis onca*), as figured in Olsen's monograph (*6*), and hyenas (*Crocuta crocuta*) (*7*) have turned-back coronoid processes. Thus, although domesticated dogs have both a turned-back coronoid process and an omnivorous diet, the presence of this morphological feature among carnivorans does not necessarily indicate an omnivorous diet.

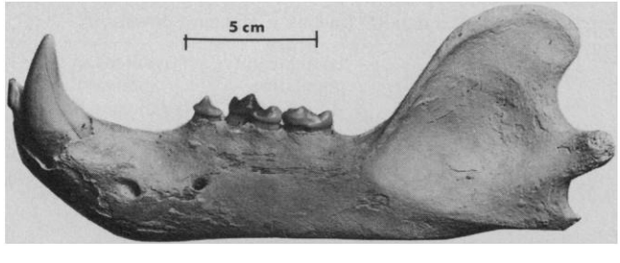

Fig. 1. Photograph of the lateral view of the polar bear (*Thalarctos maritimus*) mandible. [From Osteology Collection, Department of Anatomy, Duke University]

It should also be noted that the temporalis, masseter, and medial and lateral pterygoid muscles do not "all have their insertion on the coronoid process to one degree or another" (*1*, p. 535), as Olsen and Olsen state. In carnivorans, only the temporalis and the zygomaticomandibularis muscles insert along the coronoid process. The masseter and medial pterygoid muscles insert into, or in the region of, the angular process of the mandible; and the lateral pterygoid muscle inserts along the medial aspect of the condylar process (*8*).

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Although Hylander quoted, in part, a few of our observations regarding the overhang of the coronoid apex, he did not continue with our published statement: "The evidence suggests that more investigation is needed to determine the use and function of the overhang and the relation to diet or subsistence strategy."

Hylander does not give any explanation as to why this process varies. His photograph of *Thalarctos* depicts the entire ascending ramus with a "backward" deflection rather than just the coronoid apex as we presented it. This, in the polar bears, is also a variable condition. In carnivores, in general, no single character in a single individual is diagnostic, as most vertebrate osteologists will agree.

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