

some of these reflexes, in particular pre-absorptive insulin release, due to disease or loss of vagal innervation from surgery, have difficulty processing foods and maintaining normal blood levels of nutrients.

Concluding remarks

Before swallowing, everything a mammal samples orally will undergo a chemical analysis provided in large part by the gustatory system. What an animal ingests both in the short-term and over a lifetime has undeniable consequences on survival. So critical are taste sensations to the recognition and enjoyment of foods, and the appropriate digestion and utilization of nutrients, that humans who acutely lose their sense of taste, such as following radiotherapy, for example, often will not eat. Thus, while we may tend to take the sense of taste for granted relative to our other sensory modalities, its significance for health and quality of life should not be trivialized.

“What is it like to lose your sense of taste? To know that the most luscious fruit is a cinder, and its juice flavored with copper and bicarbonate, or that a Whitstable oyster is no more appetizing than a slug? If, by a might of effort, these ‘cinders’ are forced down with copious fluid, the consequences are acute indigestion and vomiting. The patient is not hungry anyway, and it is easier to starve.”

E.M. MacCarthy-Leventhal, *The Lancet* (1959), 1138-1139.

Further reading

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Use of stable isotopes to examine how dietary restriction extends *Drosophila* lifespan

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The ability of dietary restriction to increase animal life span is often thought to arise from differential allocation of resources between somatic investment and reproduction [1-4]. In this theory, reproduction is repressed upon dietary restriction to make scarce nutrients available to somatic functions that increase survival. Here, we label nitrogen and carbon in the dietary yeast of *Drosophila melanogaster* with stable isotopes to determine whether resources are invested to somatic tissues at the expense of reproduction. We find that females on a full diet acquire and allocate more dietary carbon, nitrogen and essential amino acids (EAA) to eggs than females on a restricted diet. Full-diet females also invest more carbon, nitrogen and EAA into somatic tissue

than those on a restricted diet. Thus, the longer lifespan of flies on a restricted diet relative to those on a full diet cannot be explained by greater absolute somatic investment, and high somatic investment does not ensure longevity. We find, however, that resource allocation to somatic tissue relative to investment to eggs is greatest in females on a restricted diet. To account for these patterns we propose that dietary restriction in *Drosophila* may extend lifespan through somatic investment relative to damage incurred from reproduction [5].

We labeled yeast acquired during larval and adult feeding with ¹³C and ¹⁵N and traced their allocation into eggs and somatic tissue when adults were maintained on restricted and full diets (4% and 16% yeast, respectively; see Supplemental Data published with this article online for methodological details). Survival was greater for females on a restricted diet, whereas females on a full diet presented 11-fold higher total fecundity (Figure S1 in Supplemental Data). To quantify the investment of resources into eggs, we estimated the proportional contribution of carbon, nitrogen, and EAA acquired from yeast (Figure S2 and S3) and multiplied this by daily fecundity, egg mass and egg composition. Females on both diets invested few larval-acquired resources to eggs. From adult-acquired nutrients,

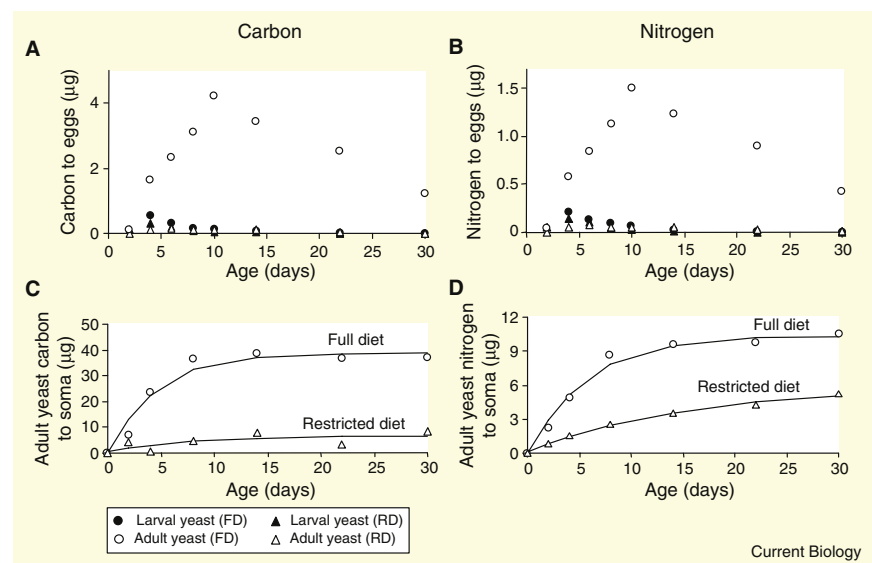


Figure 1. Daily per capita mass of carbon and nitrogen acquired from larval and adult dietary yeast, under restricted and full diets, invested in eggs (A,B), and as current content in somatic tissue (C,D).

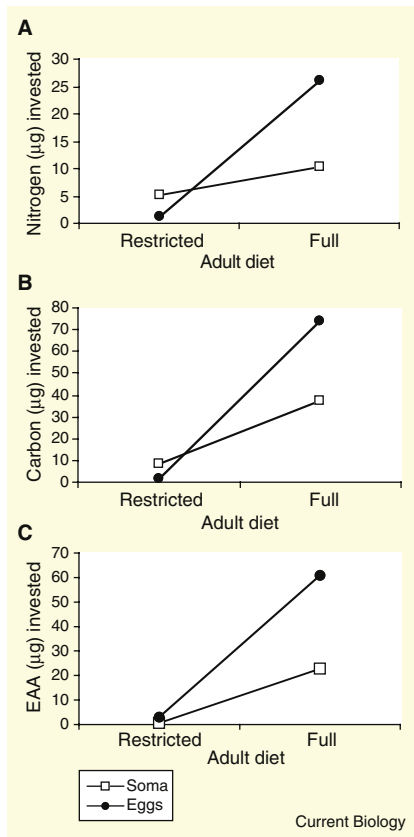


Figure 2. Total lifetime investment into soma and eggs of (A) nitrogen, (B) carbon and (C) EAA acquired from adult dietary yeast.

females on a full diet invested 39-fold more carbon, 24-fold more nitrogen and 20-fold more EAA to eggs than those on a restricted diet (Figure 1A,B and Tables S1 and S2).

We then investigated how these same resources are invested into somatic tissues. Somatic maintenance takes place through processes that defend against and repair age-related damage [6]. Somatic maintenance is difficult to define operationally. Here we assume that maintenance and repair are proportional to the synthesis and turnover of new somatic protein and other structural compounds. The incorporation of EAA from the adult diet provides a direct index of protein turnover. In addition, somatic turnover of carbon and nitrogen from the adult diet measures total resource investment to soma. Together, these rates provide a broad measure of somatic repair [7,8]. Here we quantify elemental turnover and EAA incorporation to assess somatic investment (see Supplemental Experimental Procedures).

Turnover of somatic carbon and nitrogen was greater in females on a full diet than in females on a restricted diet: full-diet females incorporated four-fold more carbon and twice as much nitrogen from adult-acquired yeast into somatic tissue compared with restricted-diet females (Figure 1C,D). These estimates of somatic turnover were determined in two ways: firstly, as the incorporation of resources from adult-acquired yeast into soma; and secondly, as the loss of larval-acquired resources from adult soma. For nitrogen, these two estimation methods produced similar results (Figure S4, Table S2). For carbon, we observed differences between incorporation and loss, which we attribute to differences in the input of carbon from adult dietary sucrose (Figure S4). Likewise, females on a full diet replaced approximately 30% of the EAA in somatic protein with EAA from their adult diet, whereas somatic incorporation of EAA from adult-acquired yeast was undetectable in females on a restricted diet (Figure S5). This effect of diet must be caused by differences in somatic protein turnover between females fed full and restricted diets, since somatic mass did not vary with age in females on either diet (Figure S6). Finally, females invested few larval-acquired resources into eggs, indicating that EAA were not incorporated from the diet to replace somatic resources that had been used for reproduction (Table S2).

These data provide a common currency to evaluate somatic and reproductive investment (Figure 2). Females on a restricted diet invest far fewer resources to reproduction, as expected, but they also invest less carbon, nitrogen and EAA to somatic tissue. Contrary to the expectation from the basic resource trade-off model of dietary restriction, we find that net somatic investment is greatest in the short-lived, full-diet females. Resource allocation can still account for the effect of dietary restriction on lifespan if we consider that reproduction incurs direct somatic damage, for instance, if the activity of egg production represses repair systems, such as heat shock proteins, or accelerates the generation of reactive oxygen

molecules [5,9,10] (Figure S7). In this situation, dietary restriction may extend lifespan if resource allocation to somatic repair exceeds the damage induced by the level of reproduction that is supported by the current nutrient intake. Our data are consistent with this interpretation: the long-lived, restricted-diet females have the greatest ratio of resource investment to somatic tissue relative to resource allocation to eggs. An alternative interpretation is that resource investment may influence aging solely through damage induced by reproduction, if processes of somatic maintenance are independent of molecular turnover and nutrient acquisition. With isotopic metabolic analysis it may be possible to distinguish between these hypotheses by identifying the specific somatic molecules that turn over when diet restriction extends lifespan and reduces reproduction.

Supplemental data

Supplemental data including experimental procedures are available at <http://www.current-biology.com/cgi/content/full/18/4/155/DC1>

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