

# Investigating the Controversy Surrounding Caloric Restrictions in Humans: Are the Potential Benefits of Slower Aging Worth the Risks?

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## Overview

### What is it?

- A defense
- Ingests too few calories to support its usual routines,
- Obtains all necessary micronutrients

### Underlying Mechanism

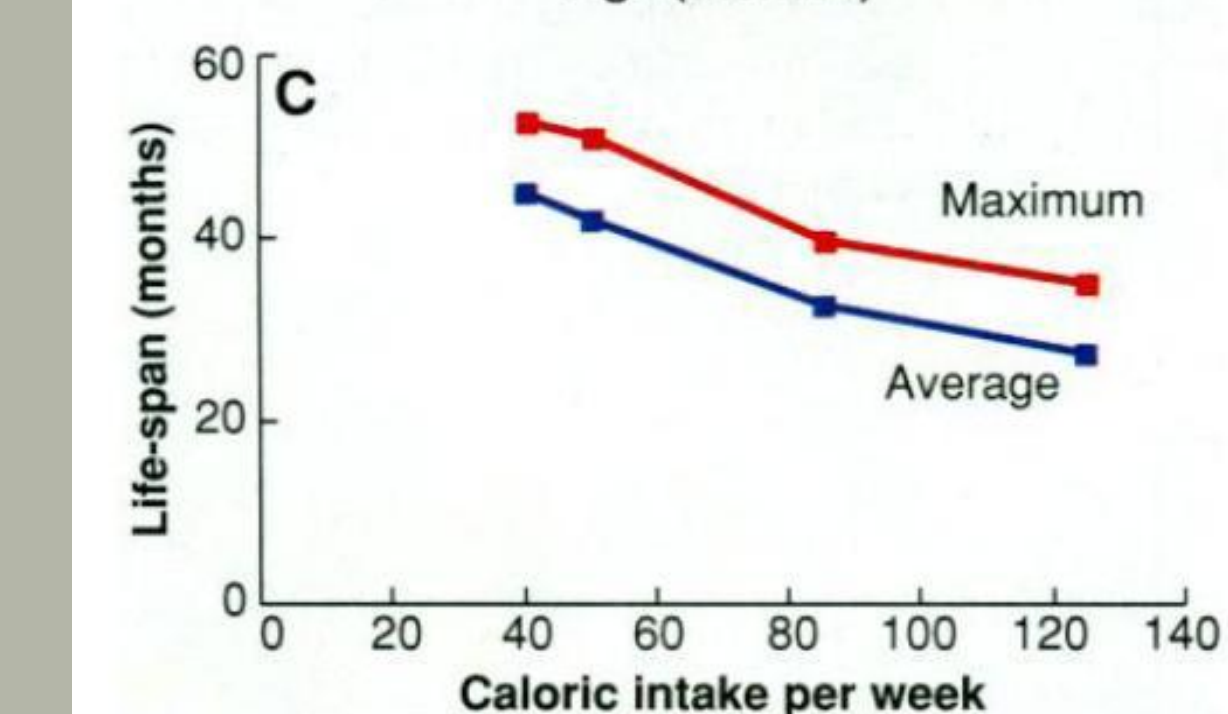
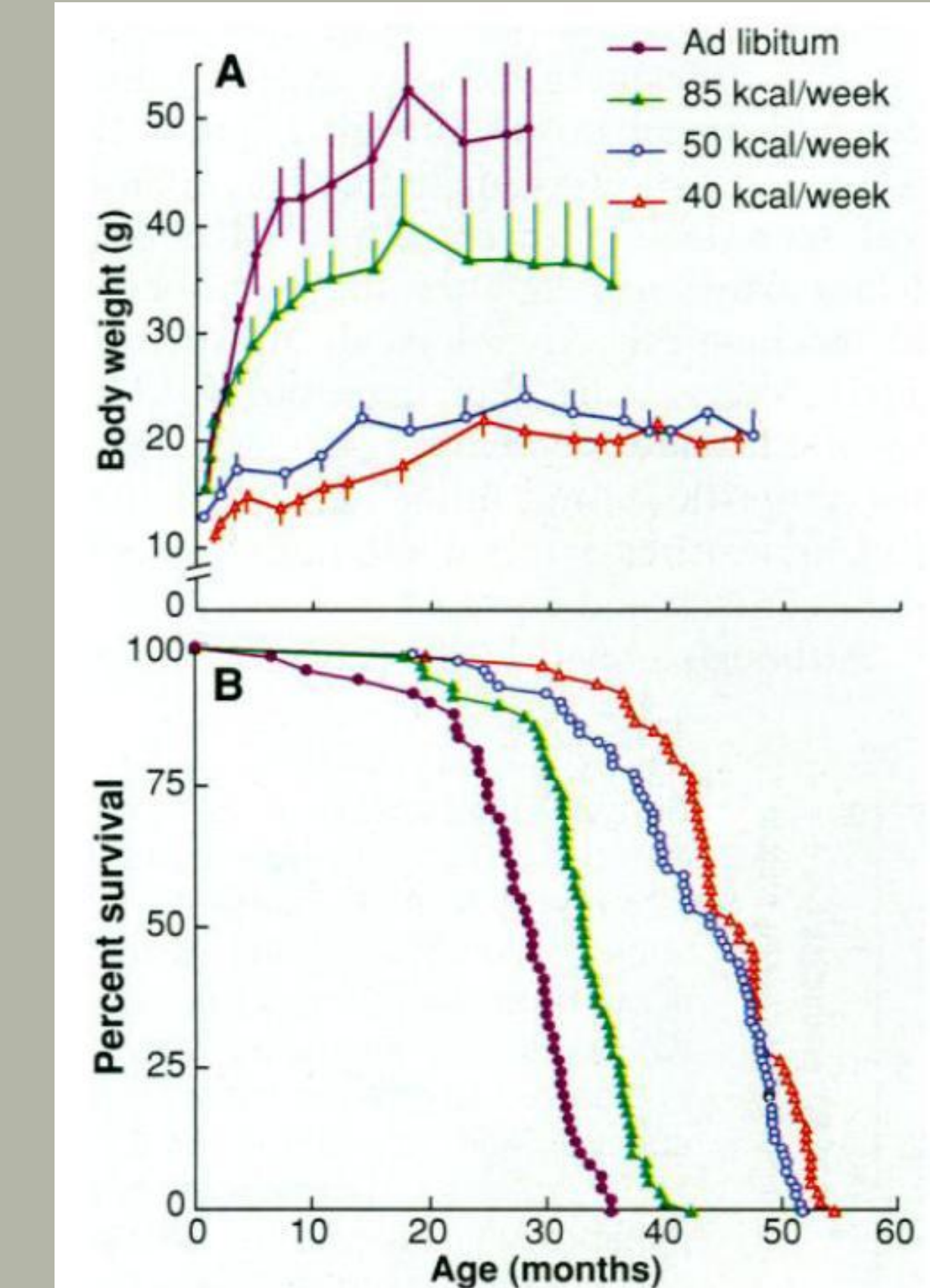
- Reduction of oxidative damage,
- Changes in hormones,
- Alterations in gene expression .
- Maintenance homeostatic mechanisms.
- Not a single factor, rather a combination

Organ System	Ad Libitum Fed	Dietary Restricted
Cardiovascular		
Severe	21	1
Moderate	0	0
Respiratory		
Severe	20	1
Moderate	12	1
Gastrointestinal		
Severe	20	2
Moderate	2	0
Hepatic		
Severe	16	1
Moderate	2	0
Renal		
Severe	6	0
Moderate	8	1

Note: Due to multiple pathology, particularly in the ad libitum-fed primates, monkeys may be represented in a disease category more than once.

The number of pathogens are greatly reduced in monkeys that were calorically restricted

- Tracks the body weight of mice since birth.
- Plots the percent survival over time based on diet.
- The fewer calories, the higher the life span



### How it relates to Aging

- Age at a slower rate
- Increase in longevity
- Greater resistance to age-related diseases
- Additional physical, behavioral, and cognitive changes take place

### Bridging the gap

- Rodents, which were the primary subjects for many CR experiments are not closely related to humans
- If the data for the rodents relates with monkeys, then the probability that the data can be applied to humans increases

TABLE 2. Summary of findings from primate caloric restriction studies

Finding	Agrees with Rodent Data
▼ Body weight	Yes
▼ Fat and lean mass	Yes
▼ Trunk: leg-fat ratio	NR
▼ Time to sexual maturity	Yes
▼ Fasting glucose/insulin	Yes
▲ Insulin sensitivity	NR
▼ Metabolic rate (short term)	Yes
▼ Metabolic rate (long term)	Yes
▼ Body temperature	Yes
◆ or ▲ Locomotion	Yes
▼ Serum triglycerides	Yes
▲ Serum HDL 2B	Yes
▼ IGF-1/growth hormone	Yes
▼ IL-6	Yes
▼ Testoster-one	NR
◆ Estradiol, LH, FSH, prog	NR
◆ Wound closure rate	Yes
◆ Fibroblast clonal proliferation	?
◆ β-gal senescent cells	?
▼ Rate of decline in DHEAS	?
▼ Lymphocyte number	Yes
◆ Lymphocyte calcium response	No

SYMBOLS: ▼, decreased; ▲, increased; ◆, no effect or change; NR, not reported.

## Physical Aspect

### When to begin

- Animal research has established that CR can begin at any time
- Recommended that it is deferred until the growth phase is completed

### Physical Reactions

- Less likely to have an active sex life along the way
- To avoid squandering energy on heat,
  - Basal body temperature is turned down
  - Better handle exposed to higher temperature
- Increased capacity for more rapid wound healing

## Behavioral Aspect

### Animals

- Activity levels in CR research specimen rise selectively at feeding time
- Depressed activity all other times
- Higher average activity score over a 24 hour period
- Aggression increases in food related activities
- Lack of information on periods other than eating, sleeping and running
- Behavior of individuals are now primarily based on the cost-benefit considerations.

### Humans

- The human subgroups likely to find CR appealing are rigorously socialized
- Inhibitions eventually begin to break down under the pressure of imposed starvation.
- The longer and more severe of CR, the more inhibitions and investments dwindle
- Parenting responsibilities are typically the last interpersonal investments to be withdrawn.
- Affects Reproduction
  - Females' libido are suppressed and there is a loss of fertility
  - Males take a hit in terms of libido, but they preserve the capacity to procreate

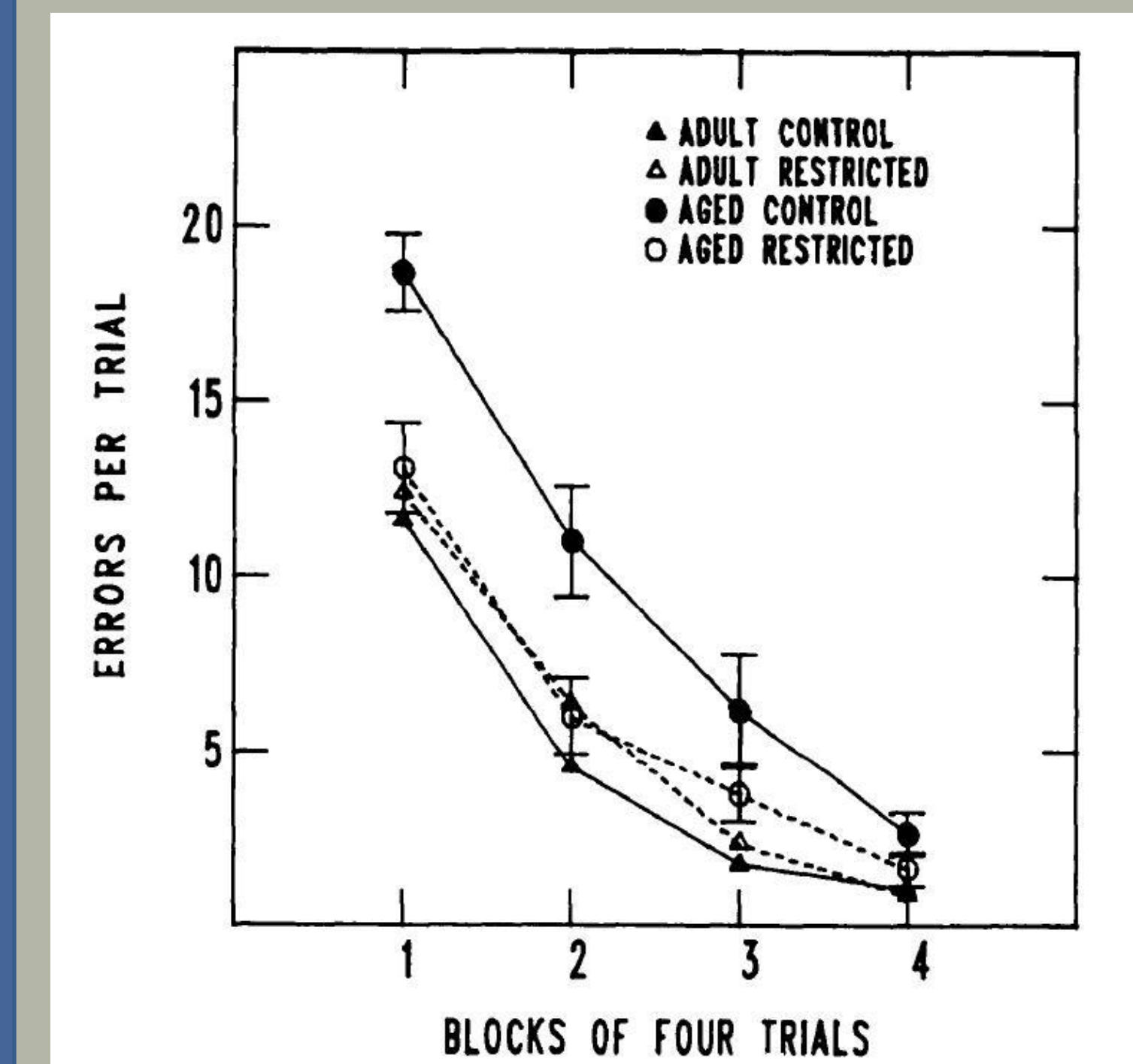
## Cognitive Aspect

### Effects on Basic Cognitive Abilities

- Largely spared
  - Even in the absence of fully satisfactory nutrition.
  - Underfed humans may feel stupid, but for the most part they do not test stupid.
- Long-term effects
- Later in life, CR rodents begin to differ such that they do not loose nearly as much cognitive function

### Effects on higher order cognitive functions

- Recent studies of on stroke Alzheimer's disease and Parkinson's disease models
  - That CR may reduce the probability of incidences
  - As well as the probability of the impairment associated with these conditions
- This is due to an increase in neuroprotective effects
  - The body will focus more on the protection of the body when faced with limited resources
- The cognitive effects most certain to afflict humans on sustained CR cannot be assessed in non-verbal animals.
- They think solely about food At the expense of abstract, creative and interpersonal thought content.
- The same preoccupations are reported by:
  - The need to plan and enforce one's own CR regimen demands the allocation of additional cognitive resources



### Cognitive Assessment

- Aged Control made significantly more errors than Aged Restricted
- Age Restricted remained at a similar error rate as the adult groups

## Implications

- We can better advise patient with AN so that they reduce their eating in a more healthy and beneficial way
- Some researchers think that the CR regimen is an ethical issue for human use
- Do humans even have the fortitude to self-apply extreme restriction?
- A more accurate overview of CR would read something like this: "Since animals (housed separately in stable, protected environments) thrive (physically) on (correct, sustained, externally controlled) CR, people will too".