

## Consumer warning label

1) Parts of what I'm about to tell you are false.

I just don't know which parts.

Every time we do a new experiment and get new results, our understanding changes. Some of the things we used to believe, we find out were incorrect.

2) For almost everything we'll talk about, there are some researchers who disagree with the conclusions. They may have done different experiments, or have different interpretations. I'll try to present what the majority of researchers understand and agree.

3) A lot of what we know about neurons, aging and the brain has come from studying animals such as worms, snails, rats, mice, and monkeys, as well as humans.

Something that works in a rat brain may not work the same way in a human brain.



- “A worm, with very few exceptions, is not a human being.”  
Mel Brooks in Young Frankenstein.

4) The best evidence that a new treatment works in humans comes from a clinical trial in which

- we compare the new treatment to a placebo (or the current standard treatment)
- patients are randomly assigned to either placebo or new treatment
- neither the patients nor the physicians know to which treatment they are assigned
- multiple clinical centers participate in the clinical trial, and the results are consistent across centers
- the study includes diverse populations (old and young, with and without concomitant disease, with and without concomitant medications, and so on)

This is a multi-center, randomized, placebo-controlled, double-blinded study. Very few interventions have been tested in this way. We make a lot of choices without such good evidence.

5) Even when a clinical trial indicates that a treatment works, that only means that the treatment works on average, for some proportion of the patients. You may not benefit.

You may respond differently to a treatment because of

- different genetics
- different environmental factors
- previous disease
- concomitant medications
- other causes

We'll see an example of a drug candidate that inhibits the brain enzyme COMT, and how the drug has opposite effects on memory for people with different COMT genetic variants.

6) Lots of evidence about how things affect your brain is based on observational studies, also called epidemiological studies. For example, there is a correlation between diet high in saturated fat and increased risk of Alzheimer's disease. But this doesn't prove that eating saturated fat causes or contributes to Alzheimer's.

It's possible that some third factor, such as a particular variant of a gene, both

- makes people eat high levels of saturated fat, and

- increases the chances that they will get Alzheimer's disease.

If there were such a gene variant, then reducing saturated fat in your diet might not reduce your chances of Alzheimer's. Correlation does not prove causality.

#### 7) Inconsistent results when testing different types of memory and cognitive abilities

There are many different types of memory and cognitive abilities:

- memory for facts
- memory for physical abilities
- memory for locations
- short term and long term
- verbal
- auditory
- speed of recall
- and many others

When researchers do experiments to see if drugs, food, supplements, or exercise affect how a brain ages, they measure only a small number of the possible types of memory and cognitive abilities that could be affected.

Experiment results may well differ, and appear to be inconsistent depending on

- what type of memory or cognitive abilities are measured
- duration and intensity of treatment
- the baseline characteristics of the subjects

If we are fortunate, the inconsistent results help refine our understanding of exactly what is happening. What types of memory is affected? In which people? At what dose?

8) What's in a supplement? Many supplements are plant products, for example green tea and ginkgo biloba. The amount of active ingredient(s) in tea and ginkgo depends on many factors, such as

- the soil it grows in
- how much water
- how much sun
- how much fertilizer
- insects and parasites
- when it was harvested
- how it was processed

- how it was stored and shipped
- how long it has been on the shelf

Because of these variables, the amount of each active ingredient can vary tremendously. This variation makes it very hard to perform clinical trials to test the effects of an herbal supplement, and may explain why clinical trials of herbal supplements often give inconsistent results.

It also makes it very hard to predict how any given batch may affect you.

A few studies have attempted to determine if the amount of active compound reported to be in a commercially-sold supplement is the actual amount. The results are often disappointing, with great variation from the claimed amount.

#### 9) Drug interactions, drug metabolism

Supplements may interact with medicine you are already taking. The supplements and drugs that you take are broken down by your body (usually in your liver) and eventually excreted (usually in urine produced by your kidneys). As we age, our livers and kidneys are likely to become less effective. We lose some ability to process and excrete these compounds. When our liver or kidneys start to decline, it is easier for toxic amounts of a drug or supplement to accumulate. This increases the risks of side effects.

Find a health care professional you can talk with to see what is best and safe for you.