The Teaberry Trial Testing The Translational Infidelity Theory of Aging

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Abstract

The Translational Infidelity Error Theory of Aging states that this is another likely cause of human aging, distinct from free radicals, inflammation, and telomere shortening. Translation infidelity may contribute to aging because translation occurs too rapidly or too slowly. As a result, incorrect amino acids are incorporated into proteins and proteins may fold or be processed improperly as, or after, they leave the ribosome. These dysfunctional proteins may be produced from incorrect charging of amino acids onto tRNAs or other downstream mechanisms with error rates exceeding 10%. Altered proteins may accumulate from mistaken charging of amino acids onto tRNAs, incorrect proofreading of amino acid incorporation, and improper folding after translation. These errors may increase when translation occurs too rapidly.

Translation may be improved by EGCG, found in green tea. EGCG may thus reduce errors in translation, increasing functional proteins, and decreasing improper folding, as is found in Alzheimer's. Blueberries provide an abundant source of polyphenols. These degrade to form quercetin. Quercetin blocks the degradation of EGCG from green tea. So consumption of blueberries, followed by drinking one cup of green tea, can increase the half-life of EGCG and decrease protein errors during translation.

The Teaberry Study has volunteers consuming blueberries, green tea, neither, or both regularly for 28 days. They take online measurements of decision-making speed, memory, and hearing throughout the 4 weeks to evaluate any changes in abilities at these tasks. Volunteers receive data on how their abilities change during their trial, and how the various groups compare. Those who wish to receive more information about volunteering may email teaberrystudy@gmail.com or visit the study home page http://www.blueberrystudy.com/teaberrystudy/.

ABBREVIATIONS AA – amino acid; EGCG - epigallocatechin gallate

Introduction

There are many theories about why humans age, what causes chronic diseases to develop, and why we eventually die. Understanding the rationale and evidence for each of these theories provides guidance on actions one can take to increase health span. The Teaberry Study is an ongoing trial, which volunteers are welcome to join, to determine whether a particular intake of blueberries and green tea may reduce the risk for translation errors (see #4 below).

Theories of why healthspan ends. The first three theories of aging listed below are well supported by scientific literature, with specific actions one can take to lessen their progression:

1. *Free Radical Theory of Aging* (1): This was proposed by Denham Harman. A host of diseases are attributable to free radicals, which are unpaired electrons causing oxidation and crosslinking of biomolecules. To lessen free radical damage, one can consume 500 mg vitamin C twice a day (2), 400 IU vitamin E twice a week, and eat a diet of colorful fruits and vegetables, coffee, tea, dark chocolate, etc. that contain a variety of antioxidants.

2. *Inflammation Theory of Aging* (or "Inflammaging") (3): This is another cause of chronic disease, including plaque in the arteries, cancer, etc. To reduce inflammation, one can consume fish oil, avoid red meat, reduce stress by exercising, limiting exposure to the media, socializing with friends, meditating and practicing yoga.

3. *Telomere Shortening Theory of Aging* (4). The length of telomeres, which are caps on the end of chromosomes, preserve our genetic information to allow longevity. Actions that shorten telomeres include stress and high metabolic rate. Consuming antioxidants, staying fit, and relaxing are all useful to keep long telomeres. Note that EGCG and quercetin help maintain telomere length (5).

4. *Translational Infidelity Theory of Aging* (6-8): The basic mechanism of Translation Infidelity is that mRNA is translated incorrectly, leading to many errors. Examples are: incorporating the wrong amino acids into proteins that then fold improperly, binding the wrong AA to tRNA or the wrong tRNA to a codon, and misreading the frame. Some results of such faulty proteins might be that they degrade, causing a shortage of needed proteins, or remain malfunctioning and accumulate as hazardous waste, such as plaque in Alzheimer's, or may accumulate as debris in the endoplasmic reticulum (9).

Processes that may prevent functional proteins from being "lost in translation" include: 1) increasing the availability of needed amino acids, 2) slowing the rate of translation to increase reading accuracy, 3) providing time for better post-translation proofreading, 4) increasing degradation of misfolded proteins, 5) diluting the accumulated damage by half through cell division or mitogenesis, or 6) recycling old organelles via autophagy. Helpful actions likely include getting exercise, eating blueberries, drinking green tea, and adjusting one's diet to include beneficial foods such as tomatoes, onions, strawberries, and cabbage. These foods contain AA ratios that are compatible with human mRNA translation requirements, which may contribute to their health benefits.

Protein misfolding is responsible for a growing list of chronic diseases, such as ALS (amyotrophic lateral sclerosis) (10). Detection by immunoassay of damage-associated molecular patterns shows oxidative damage in response to protein misfolding in the endoplasmic reticulum, which contributes to oxidative stress (11). The combination of EGCG and quercetin inhibit cancer cells in vitro (12) and in vivo may reduce endothelial dysfunction and inflammation (9),

The Teaberry Study is designed to test the hypothesis that consuming blueberries, followed by a cup of green tea, will reduce protein translation errors, producing measurable improvements in hearing, memory, and decision-making skills. The proposed mechanism is that polyphenols in blueberries will produce a high level of quercetin, which will block the degradation of EGCG in green tea. EGCG slows the rate of mRNA translation (13). This is also likely to slow telomere shortening (14). So eating blueberries, and then drinking a single cup of green tea may raise EGCG levels 4 to 8 fold more than the tea alone (6). This may be one reason that drinking green tea has been shown to be beneficial. Healthspan has been shown to increase regularly with up to 5 cups of green tea daily (15). Combined with eating blueberries, only one cup of green tea may be needed (16).

Method

The entire protocol is found at the clinical trial website:
http://www.blueberrystudy.com/teaberrystudy/ (see fig. 1). This protocol has been approved by the Beloit College IRB.

Up to 3 online measurements are selected by each volunteer. Each measurement requires 1 to 3 minutes to complete on a computer with internet access. Participants evaluate memory (see figs. 2), decision making speed, and sensitivity to hearing different tones. The first two measurements have been developed for over a decade as part of the Blueberry Health Study (BlueberryStudy.com). The hearing measurement was evaluated in collaboration with the University of Connecticut Audiology Center.

For memory, a series of 10 random faces are shown sequentially, and the person is asked to decide which among 20 random sequential faces she recognizes.

For decision making, one is shown a series of letters V or N, and asked to hit the corresponding letter on the keyboard precisely and rapidly, first using only one finger, and then using two fingers (fig. 5).

For hearing, a sequence of three notes are played, each sliding from inaudible to audible volumes and pitches (fig. 4)**.** Participants press any key as soon as each sound is heard.

After completing the informed consent, volunteers are allowed to select from four diets: A. control diet (normal but no green tea or blueberries); B. green tea (every day at least one cup); C. blueberries (every day either 1/2 or 1 cup); or D. mixed (every day either 1/2 or 1 cup blueberries, then one cup of green tea within 12 hrs).

The first diet, Phase 1, is followed for 28 days. The first week, measurements are done at least 4 different days at about the same time. Each of the next 2 weeks they are done at least once. The fourth week they are done on four different days.

Volunteers are expected to complete at least 2 phases, so comparisons can be made**.** They are encouraged to do all four phases and repeat one so consistency can be evaluated.

Each participant has a blind account that automatically stores confidential results. Results are evaluated by Dr. Rolf Martin, using Microsoft Excel and Umetrics SIMCA software (Umetrics, Kinnelon, NJ).

Figure 2: Images Recall Measurement: See Step 1 at home page (Figure 1)

Figure 1 : Study Home Page:
http://www.blueberrystudy.com/teaberrystudy/

Results
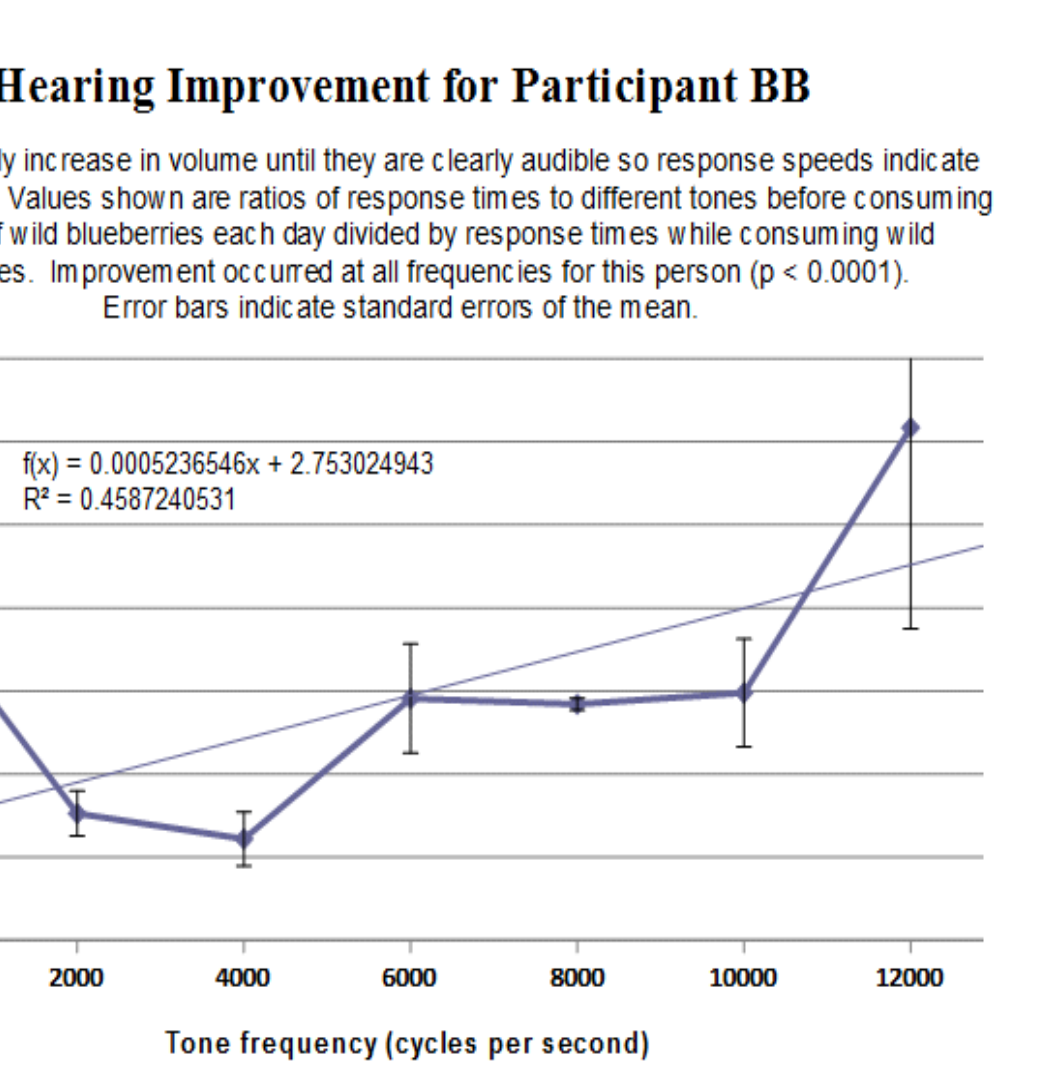
Figure 3 shows the value of the memory test, which has been used in the Blueberry Health Study. Figure 4 shows results of the hearing test after a single month eating blueberries. Figure 5 gives an example of the complete data collected for a single set of decision-making measurements by one individual throughout all four dietary phases, which need to be analyzed for decision speed. Negative numbers reflect incorrect choices.

Figure 3: Example of online memory testing

Ten Year Increase In Memory Scores For Participant I

Figure 5: Example of a single set of measurements of one individual

Two-Choice Decision Speed "Gatling Gun" Scores from Participant PV

Figure 4: Effect of one month of consuming blueberries on hearing

Hearing Improvement for Participant BB

Discussion

Now that practical strategies described in the Introduction to slow the first three likely causes of chronic disease have been developed, we are seeking additional inexpensive steps that may increase healthspan. This poster invites others to join us in informing others of proven, scientifically-justified strategies to prolong good health, and to collaborate with us to investigate a fourth likely cause and strategy. The Teaberry Trial has been developed over two years to extend the findings of the Blueberry Trial of Jim Joseph and Rolf Martin which began in 2002. Figure 3 shows effect of blueberries on memory. Figure 4 shows the effect on hearing. Figure 5 gives results for the decision speed measurement for a single individual. The introduction provides scientific evidence that protein misfolding occurs and that molecules from blueberries and green tea are likely to synergistically reduce that damage quickly enough for medically relevant physiologic effects to be detected over a 28 day period. Three tests have been selected for our trial for several reasons. They were available after development and refinement in the Blueberry Health Study. Changes in mental capacities are likely to occur within a few days. These changes are easy to measure with online tools. And the time required for volunteers to take all 3 tests in a sitting is less than 10 minutes after a few days mastering the instructions.

Additional volunteers may not only enjoy possible benefits of the blueberry/green tea diet. You and those you inform about this trial can also provide statistical validity for its likely benefit to be published and reported to a rapidly aging world population that may suffer less by just eating blueberries and drinking a cup of green tea.

Conclusion

The Teaberry Trial offers volunteers a chance to discover, with scientific proof from their results, how simple dietary changes may increase their health span and maintain or enhance their mental capacities. You may email teaberrystudy@gmail.com for information, to be alerted when the next trial begins, or if you are interested in collaborating. Please go to http://www.blueberrystudy.com/teaberrystudy/ to try the measurements.

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